Successfully treated but not fit for purpose: paying attention to chronic lung impairment after TB treatment

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SUMMARY

In 2013, 86% of patients with newly diagnosed tuberculosis (TB) successfully completed treatment and were discharged from care. However, long-term studies in industrialised and resource-poor countries all point to a higher risk of death in TB survivors than in the general population. The likely explanation is chronic restrictive and obstructive lung disease consequent to TB. We call for better linkages between TB control programmes and respiratory medicine services, a better understanding of the burden of respiratory disability at the end of anti-tuberculosis treatment, and political, programmatic, clinical and research action to improve the quality of life of affected patients.

KEY WORDS: TB; chronic restrictive lung disease; chronic airway obstruction; respiratory physicians; sustainable development goals

MR PHIRI, a 35-year-old subsistence farmer from rural Southern Malawi, has just completed 6 months of anti-tuberculosis treatment for presumed drug-susceptible tuberculosis (TB). He was human immunodeficiency virus (HIV) negative when tested at the time of registration for TB. He attended all his clinic visits and adhered to his fixed-dose combination of medications, and as his final sputum smear was negative for acid-fast bacilli, he was pronounced cured. In due course, he will contribute to that impressive global statistic of 85% or higher treatment success in persons newly diagnosed with TB.1 He no longer has TB. He was not known to have HIV infection 6 months previously and is therefore discharged from care. However, do we really know how healthy he is? Will he now be able to live a normal life with a life expectancy equivalent to someone who has never had TB?

The answer is probably no. In 1995, a cohort of 827 African patients diagnosed with TB in Zomba District, Malawi, was carefully followed up over 7 years from the time of registration, with visits paid to their village homes to ascertain whether the patients were alive or dead.2–4 At the time of registration, the mean age of the cohort was 35 years (standard deviation 12), and 77% of the cohort was HIV-positive; 181 patients were registered with HIV-negative TB. At 12 months, 124 (68.5%) were recorded as having completed treatment. Six years later, only 62 (50%) of these 124 patients were found to be alive; 57 (46%) were known to have died during these 6 years, with death having been ascertained by a visit to the patient’s home. The remaining five patients were lost to follow-up. As most of the deaths post-treatment occurred at home, no information about the cause of death was available, and verbal autopsy was not carried out. Much was made at the time about HIV-associated deaths, as Malawi was then grappling with the problem of a burgeoning HIV-driven TB epidemic. However, the National TB Programme (NTP) in Malawi did express surprise at the high mortality in HIV-negative patients, with nearly half of a relatively young cohort dead within 6 years of completing anti-tuberculosis treatment.

RISK OF DEATH AND LUNG IMPAIRMENT FOLLOWING ANTI-TUBERCULOSIS TREATMENT

Long-term follow-up studies in industrialised countries such as the United Kingdom, Denmark, the United States and Israel have also found that the risk of death in patients completing anti-tuberculosis treatment is high, with mortality rates consistently above those observed in the general population.5–8 In these studies, the relative risk of death was higher in males and younger individuals with TB than in the general population. However, as the authors pointed
out, the explanation for the higher mortality rates was speculative, and included premature death from chronic lung impairment, super-infections, including bronchopulmonary aspergillosis, lung cancer, liver disease and other comorbidities known to be associated with TB such as HIV infection and diabetes mellitus (DM).

Post-tuberculous lung impairment is one obvious cause of morbidity and mortality following successful anti-tuberculosis treatment. Nearly one hundred years ago, lung function studies in males and females with TB showed evidence of restrictive lung disease. More recent studies have shown that pulmonary TB (PTB) is associated with largely irreversible changes to bronchial and parenchymal structures, leading to distortions in bronchial vasculature, bronchiectasis, emphysema and fibrosis. A restrictive pattern of lung disease is common and is independent of tobacco smoking. Although pulmonary impairment is more likely after extensive parenchymal involvement, significant declines may also be observed in patients with localised PTB. Chronic airway obstruction can also be a result of PTB, and this association has been known about for over 50 years. A recent study in Mexico found that just over one third of patients with a history of PTB had non-reversible chronic airway obstruction that was independent of smoking history and impacted significantly on quality of life. Airway obstruction in these patients was significantly associated with extensive pulmonary radiographic changes, residual lung cavities and mediastinal retraction. However, similar to patients with restrictive airways disease, TB patients with no sequelae on chest radiography may also show chronic airway obstruction and persistent respiratory symptoms. In a large, recently published, international population-based study by BOLD (the Burden of Obstructive Lung Disease), the risk of restrictive airways disease and airflow obstruction in people with a history of TB was more than twice as high as that found in persons with no history of TB; this was particularly apparent in people from low- and middle-income countries.

TUBERCULOSIS AND CHRONIC LUNG IMPAIRMENT IN THE ‘END TB STRATEGY’ AND SUSTAINABLE DEVELOPMENT GOALS

The aims of anti-tuberculosis treatment, as stated by the World Health Organization in their 2010 treatment guidelines, are to cure the patient, prevent death, prevent relapse, reduce transmission of TB and prevent the development and transmission of drug resistance. The Stop TB (and now the End TB) strategy generally does a good job in achieving these aims, with treatment success in newly registered TB patients worldwide reaching 86% in 2013. However, within these broad aims there are also explicit statements about restoring quality of life and productivity and preventing death from the late effects of TB. Responsibility towards patients with PTB should not, therefore, end with attainment of microbiological cure.

The last two decades have seen an inexorable rise in non-communicable diseases in all countries of the world, with the global number of deaths from these diseases increasing from an estimated 27 million in 1990 to nearly 35 million by 2010. The term ‘non-communicable diseases’ covers a large number of conditions, but the emphasis has been on four main groups of diseases for the prevention of premature mortality—cardiovascular disease, cancer, DM and chronic respiratory disease. In the new Sustainable Development Goals (SDG), which are set to dominate global health policy from 2016 to 2030, the fourth target of the only SDG focusing on health (SDG 3.4) is ‘to reduce by one third premature mortality from non-communicable diseases through prevention and treatment by 2030’. Considerable recent attention has been focused on cardiovascular disease and DM, although chronic obstructive pulmonary disease is the third leading cause of mortality worldwide. Bronchodilators (short-acting and long-acting beta-2 agonists and anti-muscarinics) and anti-inflammatory drugs (inhaled corticosteroids and phosphodiesterase inhibitors), either singly or in combination, can provide symptomatic relief; these effects may be further augmented by persuading patients to quit smoking.

LINKING NATIONAL TUBERCULOSIS PROGRAMMES TO RESPIRATORY MEDICINE SERVICES

Given the strong association between TB and impaired lung function, there needs to be more thought and discussion about how to better link TB control programmes with respiratory medicine services and a better understanding of the burden of respiratory disability at the end of anti-tuberculosis treatment. Approximately 5 million TB patients complete treatment successfully each year; however, we have no information about the proportion of patients with respiratory disability, the severity of lung impairment or the impact on quality of life, or whether respiratory dysfunction is amenable to treatment. This needs to change. Already we are seeing connections, synergies and benefits of integrating care for communicable and non-communicable diseases, with notable examples being DM and TB.
and HIV and cardiovascular disease. TB and chronic respiratory disease need to follow suit.

For a start, NTPs need to systematically reach out to respiratory physicians, and respiratory physicians with an interest in TB need to link up with NTPs. Together these two groups need to work out simple strategies for assessing patients for lung function at the end of treatment. In high TB burden countries, sufficient numbers of trained respiratory physicians who have the necessary skills to handle the large patient load will be required. The outreach between NTPs and respiratory physicians should be combined with significant advocacy and awareness efforts to ensure that the rhetoric about linkage is matched with action.

If lung function is impaired, appropriate treatment needs to be instituted, and, ideally, patients should then be regularly followed up. Based on the cohort analysis reports of case finding and treatment outcomes, the respiratory disease burden at the end of anti-tuberculosis treatment can be measured and plans made for the treatment and management of patients. Post-treatment connections are not new to TB control programmes: for example, patients with HIV-associated TB are often discharged from TB care at the end of anti-tuberculosis treatment and referred for long-term HIV care and treatment with antiretroviral therapy. Much useful research could be carried out in this context, particularly in terms of understanding baseline risk factors that predict long-term lung damage, which may then be prevented by earlier diagnosis and, possibly, judicious use of anti-inflammatory drugs or immune-therapeutic approaches during anti-tuberculosis treatment. TB and chronic lung disease are an example of a communicable and a non-communicable disease occurring in the same patient population, although temporarily related, and we should not ignore the long-term consequences of this infectious disease. To be effective, we will need to harness and secure political, programmatic, clinical and research commitment for integrated and sustainable action.

References

En 2013, 86% des patients avec une tuberculose (TB) récemment diagnostiquée ont achevé avec succès leur traitement et ont terminé leur prise en charge. Cependant, les études à long terme dans des pays industrialisés et des pays à faibles ressources soulignent un risque majoré de décès chez les survivants de la TB par comparaison à la population générale. L’explication plausible est une atteinte chronique restrictive et obstructive des poumons consécutive à la TB. Nous plaidons pour de meilleurs liens entre les programmes de lutte contre la TB et les services de pneumologie, pour une meilleure compréhension du poids des atteintes respiratoires à la fin du traitement antituberculeux et pour une action politique, programmatique, clinique et de recherche afin d’améliorer la qualité de vie des patients affectés.

RESUMEN

En el 2013, 86% de los pacientes con un nuevo diagnóstico de tuberculosis (TB) completaron eficazmente el tratamiento y se dieron de alta del programa de atención. Sin embargo, los estudios a largo plazo en países industrializados y en países con escasos recursos indican un mayor riesgo de muerte en los pacientes que sobreviven a un episodio de TB, al compararlos con la población general. Una explicación posible es la aparición de enfermedad pulmonar restrictiva u obstructiva como consecuencia de la TB. El artículo recomienda establecer vínculos más eficaces entre los programas de control de la TB y los servicios de neumología, mejorar la comprensión de la carga de morbilidad por discapacidad respiratoria al final del tratamiento antituberculoso y adoptar medidas políticas, programáticas, clínicas y de investigación encaminadas a mejorar la calidad de vida de los pacientes afectados.