HIV and tuberculosis co-infection programmes

KEY POINTS:

• People living with HIV who have a low CD4 count are at a much higher risk of falling ill from TB infection than HIV negative people.

• It is important to offer both HIV testing to TB patients and TB diagnosis in HIV patients. Early detection and effective treatment are essential to preventing TB-associated deaths.

• WHO and UNAIDS have strongly advised countries to ensure that HIV programmes integrate regular TB screening, preventive therapy and early treatment.

Explore this page to find out more about reducing the burden of HIV in people with TB, reducing the burden of TB in people living with HIV, the progress in implementing HIV/TB programmes and implementation challenges.

In 2015, there were an estimated 10.4 million new tuberculosis (TB) cases, 1.2 million (11%) of these were among people also living with HIV.1

The two infections are strongly linked. Whereas individuals with healthy immune systems may not fall ill from TB infection, people living with HIV with a low CD4 count are at greater risk of TB infection. In fact, the risk of developing active TB is estimated to be 26 and 31 times greater in people living with HIV than in those who are HIV-negative.2

In 2014, tuberculosis surpassed HIV as the world's leading infectious disease killer, a worrying trend for a disease that is essentially treatable and curable. Moreover, TB remains the leading cause of death among people living with HIV, accounting for around one in three AIDS-related deaths.3

There were an estimated 1.4 million TB deaths in 2015, and an additional 400,000 deaths resulting

from TB among people living with HIV[4], including 40,000 children.[5] Eight countries — the Democratic Republic of the Congo, India, Indonesia, Mozambique, Nigeria, South Africa, the United Republic of Tanzania and Zambia — account for around 70% of all TB deaths among people living with HIV.[6]

The 2016 United Nations Political Declaration on Ending AIDS included a goal to reduce TB-related deaths among people living with HIV by 75% by 2020. However, as of 2017 the global HIV response is not on target to reach this goal.[7]

Along with the World Health Organization (WHO), UNAIDS has called for “urgent action” on this issue, advising countries to integrate HIV and TB services by ensuring HIV prevention and treatment programmes include regular TB screening, preventive therapy and early treatment.[8]

Reducing the burden of HIV in people with TB

It is unacceptable that so many people living with HIV die from tuberculosis, and that most are undiagnosed or untreated. Only by stepping up collaboration between HIV and tuberculosis programmes to accelerate joint action can the world reach its critical HIV and tuberculosis targets.

- Michel Sidibé, Executive Director of UNAIDS[9]

In 2014, around 11% of HIV-positive TB patients died, compared with 3% of HIV-negative TB patients.[10] Early detection and effective treatment are essential to prevent TB-associated deaths, especially among people living with HIV.[11]

Despite this, around 57% of HIV-associated tuberculosis cases remained untreated in 2015 as weak health systems continue to result in missed opportunities to diagnose tuberculosis among people living with HIV. Inadequate linkages to care after HIV or TB diagnosis, poor tracking of people, loss to follow-up and failure to reach the people most at risk of disease — including people who inject drugs, prisoners and migrant workers — contribute to the lack of progress.[12]

Increasing knowledge of HIV status

HIV testing and counselling (HTC) is recommended both for those with diagnosed TB and those with signs and symptoms consistent with TB infection. Combining HIV testing and TB facilities has been shown to increase the uptake of HTC.[13]

While the rate of testing has increased 18-fold since 2004, in 2015 only 55% of TB patients had a documented HIV test. Coverage is highest in Africa, where 81% of all TB patients had a documented HIV test result, but this varies between countries.[14] Africa is also the region with the highest proportion of people with TB also living with HIV. An estimated 31% of people with TB are living with HIV in the region. This proportion exceeds 50% in some parts of southern Africa.[15]

Starting antiretroviral treatment

Programmes need to ensure that people with active tuberculosis who are diagnosed with HIV begin antiretroviral treatment (ART) as soon as possible, preferably within integrated services or TB

facilities. ART reduces the risk of TB infection in people living with HIV by 65%.16 Data from almost 40,000 patients with HIV/TB co-infection in South Africa showed that people who received ART had almost half the risk of death than others, with particular benefit for those with a CD4 count below 350.17

A national study from Malawi found increased TB prevalence in the country which began in 1985 to be strongly associated with the advent of HIV, with TB's relative curtailment linked to the scale-up of ART. It traced the start of the continuous decline in TB in the country to 2005, 1 year after national scale-up of ART had begun.18

ART also prevents the progression of HIV, reduces the chances of another opportunistic infection that could make management of care more complicated, and reduces the chances of TB recurring. However, treating both conditions at the same time can be challenging because of side-effects, pill burden, and drug interactions.

The proportion of TB patients known to be living with HIV accessing ART was 78% globally. This is an increase from 36% in 2005. In the 30 high TB/HIV burden countries, 80% of the TB patients known to be living with HIV were on ART and in six of these countries (India, Kenya, Malawi, Mozambique, Namibia and Swaziland) the figure was more than 90%.19

In contrast, there were nine high TB/HIV burden countries (Brazil, Chad, China, Congo, Ghana, Guinea-Bissau, Indonesia, Liberia, and Myanmar) in which less than 50% of TB patients living with HIV had access to ART in 2015.20

In Côte d'Ivoire, national care guidelines recommend that people who test positive for HIV are screened for TB and initiated on TB treatment before they begin ART, in line with WHO guidance. Yet a study of more than 3,500 adults starting ART during 2004–2007 at 34 health facilities in the country found low screening rates overall with wide variations between facilities. Around 2% of those testing positive for HIV during the study were already on TB treatment, of the remainder, just 36% received some form of TB screening. Of these, 11% were diagnosed with TB and started TB treatment before beginning ART.21

Co-trimoxazole preventative therapy

Another important element for individuals with co-infection is co-trimoxazole preventive therapy (CPT), an agent that prevents a range of secondary bacterial and parasitic infections.

Uptake of this daily medication has improved considerably in recent years, reaching 87% of tuberculosis patients living with HIV.22

A study of primary healthcare clinics in Zimbabwe echoes this, reporting 88% of people diagnosed with HIV and TB coinfection initiated on CPT and 90% initiated on ART. Interestingly, the study found just 38% of people diagnosed with HIV (rather than HIV/TB) were started on ART and 40% on CPT.23

Reducing the burden of TB in people with HIV

Despite progress in providing TB preventive treatment to people living with HIV, much more remains to be done. Of the 30 high TB/HIV burden countries, 21 did not report any provision of preventive treatment in 2015. In the nine high TB/HIV burden countries that did report data, coverage among people newly enrolled in HIV care ranged from 2% in Indonesia to 79% in Malawi. 24 In order to reduce the burden of TB, the WHO recommends an approach known as the Three I's – intensified case-finding, isoniazid preventive therapy and infection control.25

Intensified case-finding

Just as it is important to offer HIV testing to TB patients, it is vital to improve the diagnosis of TB in HIV patients.

Many studies have reported high rates of undiagnosed TB in people living with HIV. All people living with HIV should be regularly screened for TB symptoms, including cough, fever, weight loss or night sweats. If any of these symptoms are present, they may have active TB and should be further evaluated.

However, appropriate diagnostics are not always available, as TB activist Blessima Kumar explains:

> When I started feeling ill, I was in a small town in southern India. I really couldn't get anyone to diagnose me properly. Then, the doctors put me on treatment anyway — without a confirmed diagnosis. I took the treatment for six months without knowing whether it was TB or not. So getting access to an accurate diagnosis was definitely one of my biggest challenges.[26]

Historically, TB has been diagnosed by looking for evidence of TB bacteria either through the use of the chest X-ray, through sputum smear microscopy, or through the culturing of bacteria. However, each of these TB tests has their disadvantages. The newer GeneXpert test can dramatically improve case finding and is recommended as the diagnostic test for people living with HIV who have a cough, fever, weight loss or night sweats.[27]

GeneXpert is a self-contained testing unit which does not require a sophisticated laboratory set up and can provide results within two hours. Using a sputum sample, the molecular test diagnoses TB by detecting the presence of TB bacteria, as well as testing for resistance to the drug rifampicin – a likely indication that the individual has multi-drug-resistant tuberculosis (MDR-TB).[28]

Some countries including Ethiopia and South Africa have made the test available at primary healthcare facilities where it has substantially improved TB diagnosis rates for people living with HIV.[29] However, in many other countries the test is restricted to secondary and tertiary healthcare facilities. It may be primarily used to diagnose MDR-TB, rather than being routinely used for case-finding in patients living with HIV.[30]

Isoniazid preventive therapy

In order to prevent cases of latent TB infection (where a person's immune system is able to keep TB under control) from progressing to active TB (causing illness), people with HIV need both prompt initiation of ART and isoniazid preventive therapy (IPT).

The latter intervention involves taking the TB drug isoniazid daily for at least six months to prevent progression to active TB. Studies conducted in Brazil and South Africa show up to a 90% reduction in TB risk among people living with HIV who have latent TB infection who receive both ART and IPT.[31] [32]

While more recent studies find IPT to be beneficial, researchers have associated it with a smaller risk reduction. For example, a study in Jimma, Ethiopia found IPT use was associated with a 50%

reduction in new cases of tuberculosis among people living with HIV who were enrolled in pre-ART care.33

A study of more than 18,500 South African gold miners working in areas with high levels of TB and HIV who had undergone IPT found that the protective effect of IPT was lost within 6–12 months of the treatment ending. This is one of only a few studies to specifically address the durability of IPT's preventative effects and suggests that persistent latent infection plays a role in the rapid return to TB incidence.34

While provision of isoniazid has grown rapidly since 2008 – especially in South Africa – across the world less than a million people living with HIV received it in 2014 (compared to 15 million people receiving ART). Two-thirds of high HIV/TB burden countries do not provide IPT as part of their HIV response.35

Infection control

The third 'I' is infection control measures in healthcare facilities and other settings where people with TB and HIV are frequently crowded together. This is to ensure that both people receiving HIV care and the staff providing it are not exposed to TB in the process.

A study examining infection control measure in TB-designated hospitals in Zhejiang Province, China found just under half (49%) were monitoring TB infection control in high-risk areas, 42% had introduced shorter waiting times for people with TB, and 46% provided a separate waiting area for patients with suspected TB. Effective respirators were available in 97% of hospitals, although just half checked these respirators regularly.36

Similarly, a study of infection control measures implemented by facilities in Ugu and Uthungulu health districts of Kwazulu-Natal province, South Africa found levels of relatively low compliance. Overall, 18 out of 37 infection control measures were complied with by around 80% of facilities surveyed.37

Progress in implementing HIV/TB programmes

Between 2000 and 2014, joint TB/HIV activities saved an estimated 6.5 million lives. However, much more needs to be done to ensure universal access to integrated TB/HIV services and eliminate HIV-related TB deaths.38

Of those people with TB who were known to be living with HIV in 2015, 78% were initiated on ART.39

Between 2013 and 2014, the number of people screened for active TB increased from 5.5 million to 7 million in 2014. Among the 57 countries that reported data in 2015, 910,000 people living with HIV received IPT, up from 600,000 in 2013 but a slight decrease from 930,000 in 2014.40

India

India is a country with the highest burden of tuberculosis in the world, a high HIV prevalence, and high rates of HIV-associated TB.41 While the TB epidemic is countrywide, the HIV epidemic is concentrated in a few states.42

In its 2016 Global TB Report, the WHO increased its estimates of the burden of TB disease in India for the period 2000–2015, compared with those published in previous reports. This follows accumulating evidence, taken from surveys and routinely collected TB data, that previous estimates of cases and deaths were too low.43

The number of new TB cases per year in 2015 is now estimated at 2.8 million. Previously these had been set as 1.7 million, suggesting that only 59% of incidence was officially reported orginially. This new estimate is interim in nature, a more definitive assessment will follow the completion of a national Indian TB prevalence survey scheduled for 2017/2018.44

What is known is that, nationally, about 5% of people with TB in India also have HIV. However, in high prevalence states and districts, HIV prevalence among people with TB ranges between 10-40%. Thus, while the country is dealing effectively with its HIV burden, a TB associated HIV epidemic is posing great challenges.45

India's National AIDS Control Programme (NACP) and the revised National TB Control Programme (RNTCP) have been instrumental in reducing the burden of HIV and TB. Since 2001, they have implemented collaborative TB/HIV activities.46

The national HIV/TB response includes intensified TB case finding in HIV care settings, intensified, integrated TB-HIV packages for patients, and a focus on TB prevention for people living with HIV. 47

These activities were initially launched in the six high HIV burden states. The adoption of the national TB/HIV policy framework in 2007 lead to a nationwide scale-up of joint TB/HIV programmes, which was achieved in 2012.48 It has seen cross referrals for HIV/TB increase from 120,000 in 2013/14 to 168,300 in 2014/15.49

India's experience shows how collaboration can enable the scaling up of TB/HIV programmes and promote shared ownership of interventions. It also demonstrates that political and administrative commitment is critical.50

South Africa

South Africa also has a high HIV/TB burden, and has also made robust efforts to tackle the two diseases simultaneously.

In 2009, tuberculosis was integrated into the mandate of the South African National AIDS Council (SANAC), alongside HIV and a joint HIV, TB and STI national strategic plan was developed.51

This policy has stipulated integration of HIV and TB services nationwide, by the co-location of services. In fact, 59% of people living with HIV worldwide who received isoniazid preventive therapy in 2014 were in South Africa.52

In its 2014/2015-2016/17 performance plan, the South African Department of Health reports that 60% of people with TB in the country are HIV positive. It also reports increasing incidence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB. 53

There remain significant disparities between provision in urban and rural areas. Factors affecting provision in rural areas include staff unqualified to address HIV and TB, drug stock-outs, and inadequate infrastructure (such as a lack of private rooms to conduct pre- and post-test counselling).54

Implementation challenges

The treatment gap

Although significant progress has been made in the past decade, health services do not always work in integrated ways and may even fail to provide screening for common co-infections.55

In 2015, 78% of people living with HIV who were also diagnosed with active tuberculosis were placed on ART.56 However, by contrast, just 47% of people on ART were screened for TB, 51% of people diagnosed with TB were tested for HIV, and only half of people living with HIV who developed TB were diagnosed and provided with TB care.57

Currently, the success rate of TB treatment is lower for people living with HIV (75%) whose immune systems are already compromised, than for those who are HIV-negative (83%).58

Globally, the proportion of TB patients who died during treatment was about four times higher among HIV-positive TB patients (11% versus 3%).59

The WHO recommends that treatments for common co-infections should generally be provided at the same time as treatment for HIV and the care carefully co-ordinated – for example, the possibility of drug interactions needs to be managed.60

Funding for TB/HIV programmes

In 2016, annual global funding for TB was almost US $3 billion short of what was required.61

The Stop TB Partnership's Global Plan to End TB, which covers the period 2016–2020, estimates that, in low- and middle-income countries, US$ 52 billion is required over 5 years to implement interventions that are currently available. The amount required is expected to increase from US$ 8.3 billion in 2016 to US$ 12.3 billion in 2020. Most of this funding is for drug-susceptible TB (e.g. US$ 6.4 billion in 2016), although the amount for MDR-TB is expected to double from US$ 1.7 billion in 2016 to US$ 3.6 billion by 2020; the remainder is for TB/HIV interventions. Over the same period, a further US$ 6 billion is needed for high-income countries, and an additional US$9 billion is needed for TB research and development.62

TB funding is dwarfed by HIV and malaria funding. The latest data from the Organisation for Economic Co-operation and Development (OECD) shows totals of US$ 5.4 billion for HIV, US$1.7 billion for malaria and US$ 0.7 billion for TB in 2014.63 To provide some context for these amounts, the latest estimates (for 2013) of the burden of disease in terms of disability-adjusted life years lost due to illness and death are 69 million for HIV/AIDS, 50 million for malaria and 65 million for TB.64

Furthermore, this funding is not appropriately allocated, with only 6% of the annual available funds being directed towards HIV/TB co-infection activities.65
Despite having far fewer resources, national TB programmes include more TB/HIV activities than national HIV and AIDS programmes.66 HIV grants have been found to be 59% less likely to fund TB/HIV activities when compared with TB grants.67

Considering the huge overlap between these two infections, funding needs to be scaled up in order to successfully tackle both TB and HIV.68

Multi drug-resistant TB (MDR-TB)

One of the greatest challenges faced by both TB programmes and joint HIV/TB programmes, is MDR-TB - strains of TB that are resistant to the drugs isoniazid and rifampicin.

In 2015, there were an estimated 480,000 new cases of MDR-TB. In the same year, the number of people enrolled on treatment for MDR-TB globally was 124,990, an increase of 13% from 110,587 in 2014. There was a 14% increase in enrolments between 2014 and 2015 in the 30 high MDR-TB burden countries, with increments amounting to more than 1000 patients in China, India, the Philippines, the Russian Federation and Ukraine.69

In Ukraine 22% of new TB cases are MDR-TB and 56% of people requiring re-treatment have

MDR-TB. Globally, levels of drug resistance in people presenting for TB treatment for the first time are much lower at 3%, but 20% of individuals who have previously been treated and require re-treatment have MDR-TB.70

A total of 127 countries and territories reported treatment outcomes for people started on MDR-TB treatment in 2013. Overall, the proportion of MDR-TB patients in 2013 who successfully completed treatment (i.e. cured or treatment completed) was 52%: 17% died, 15% were lost to follow-up, 9% were determined to be treatment failure and 7% had no outcome information.71
As Ethiopian activist Endalkachew Fekadu explains, the most widely used treatments for MDR-TB have considerable side-effects:

> There were eight pills and an injection each day. They were so toxic, with many adverse effects. I remember my mama waking me up every morning to take me to hospital because sometimes I just vomited all night and became faint.72

To address MDR-TB more effectively, in May 2016, the WHO recommended a new drug regimen that shortens the treatment period from two years to nine months. It also recommends a rapid diagnostic test, which can detect how resistant the patient's form of TB is and the drugs are less toxic.73

As of 2015, at least 23 countries in Africa and Asia had introduced shorter regimens for treatment of MDR-TB, which have achieved high treatment success rates (87–90%) under operational research conditions.74

It is hoped that these developments will lead to fewer interruptions in treatment and reduce the number of people who are lost to follow-up.75

Drug access and prices

MDR-TB puts a particular burden on already stretched health systems. Whereas treatment for drug-susceptible TB may cost between US$ 100 and US$ 1,000, the price tag for treating MDR-TB is typically US$ 2,000 to US$ 20,000.76

After decades without new drugs in the pipeline, an opportunity has arisen with the introduction of new drugs bedaquiline and delamanid, as well as the re-purposing of drugs licenced for other conditions such as linezolid and clofazimine.

By the end of 2015, 70 countries had started using bedaquiline and 39 countries were using delamanid.77 However, these remain largely unaffordable in low- and middle- income countries, with manufacturers often having little interest in the drugs being more widely used for TB treatment in high-burden countries.78

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