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People living with HIV at higher risk of multi-drug TB

A major study led by researchers at the University of Cape Town's (UCT) School of Public Health found that people living with HIV (PLHIV) are at a higher risk of developing multi-drug or rifampicin-resistant tuberculosis (MDR/RR-TB) than HIV-negative individuals – with those living with advanced HIV up to three times more likely to develop the resistant strain.

Resistance against rifampicin, one of the most effective first-line drugs for TB treatment, poses a serious challenge, rendering the standard short-course regimens ineffective and leading to longer, more complex and toxic treatments with poorer outcomes and increased mortality.

South Africa ranks among the top 20 countries with the highest burden of TB, HIV-associated TB and MDR/RR-TB in the world. The extent to which acquired MDR/RR-TB during treatment is driving the MDR/RR-TB in the country is unknown. Although an association between HIV and MDR/RR-TB is known, it is not well understood whether this is primarily due to acquired resistance during treatment or direct transmission, as few studies have distinguished between the two.

"It is also vital to understand whether drug resistant TB (DR-TB) is still being created, in order to determine the best way to tackle the DR-TB problem. If DR-TB is still being created through inadequate treatment of HIV-associated TB, then improvements for treatment of normal or drug-susceptible TB is critical. Otherwise, the cycle of diagnosing and treating DR-TB will continue into the future, with enormous impacts on individuals and the health system," said Nesbert Zinyakatira, lead author of the study and PhD student in UCT's Division of Medical Microbiology.

Published in *eClinicalMedicine* under the title "Impact of HIV and hospitalization on the incidence of subsequent rifampicin-resistant tuberculosis after initiation of first-line tuberculosis treatment: a retrospective cohort study in South Africa", the study analysed routine health data from over 190 000 individuals in the Western Cape public health sector – one of the largest cohorts ever studied in a high TB and HIV burden setting.

The findings showed that prolonged hospitalisation increased the risk of developing MDR/RR-TB compared to non-hospitalised individuals regardless of HIV-status. PLHIV hospitalised for more than a week were four times more likely to develop MDR/RR-TB, while HIV-negative individuals were three times more likely.

"Hospitalised individuals are typically more ill and often have compromised immune systems either due to HIV or other comorbidities such as diabetes or hypertension, which require ongoing care. This makes them more vulnerable to infections, particularly nosocomial (healthcare-acquired) transmission, especially when infection and prevention control measures are inadequate," explained Zinyakatira.

The study recommends improving TB treatment for PLHIV through a more individualised approach that considers variations in clinical characteristics such as disease severity, comorbidities, and body weight. According to Zinyakatira, increasing rifampicin dosages has been suggested as this is safe, and associated with improved treatment outcomes, including reduced rates of treatment failure, relapse and mortality in recent trials of TB treatment.

Zinyakatira said infection control measures in health care settings that can help reduce the transmission of drug-resistant TB include increasing ventilation and reducing overcrowding in settings where people with undiagnosed and untreated TB are likely to be present. "Ensuring that people who may have TB are rapidly and effectively diagnosed and placed on treatment is also key, given that treatment will reduce TB infectiousness. Other measures include regular staff screening, staff and patient education, and the use of protective equipment where feasible for staff and patients such as N95 respirators and masks," he added.

Based on the findings, Zinyakatira said PLHIV and those with other comorbidities may need individualised TB treatment approach and intensified monitoring for treatment response to minimize risk of drug-resistance TB.

"The findings are generalisable to most high HIV and TB burden countries in sub-Saharan Africa and beyond, where some of the TB and HIV programmes have limited resources. There are important lessons for these countries which include the need to monitor drug-resistance, improve access to newer and shorter treatment regimens, and strengthen integrated healthcare services for HIV, TB and other comorbidities," he said.

Addressing the overlap between HIV, hospitalisation and drug-resistant TB is critical to achieving global TB goals, said Zinyakatira. "TB co-infection with HIV including other comorbidities complicates treatment due to drug–drug interactions, often leading to poor adherence and treatment outcomes. In addition, individuals that are sicker are more likely to be hospitalised, and their weakened immune systems increases the risk of drug-resistant transmission, especially in healthcare settings with inadequate infection and prevention control measures."

He concluded: "Policymakers and healthcare providers should prioritise enhanced screening, prevention and treatment, and closer monitoring strategies for TB, especially among PLHIV and hospitalised individuals due to the increased risk of MDR/RR-TB. This includes tailored drug regimens, intensified treatment monitoring, individualised treatment for those with weakened immune systems, and strengthening infection and prevention control measures in healthcare settings."

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