Fluoroquinolone Resistance in Drug-Resistant Tuberculosis, Kharkiv, Ukraine, 2019–2023

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DOI: https://doi.org/10.3201/eid3103.241675

Rifampin-resistant *Mycobacterium tuberculosis* was identified by the World Health Organization as a pathogen of public health critical importance. During 2014–2023, an increase in fluoroquinolone resistance in rifampin-resistant *M. tuberculosis* from Kharkiv, Ukraine, was observed. Efforts to mitigate factors contributing to resistance should be prioritized to prevent further escalation of that threat.

In 2024, the World Health Organization (WHO) officially recognized rifampin-resistant *Mycobacterium tuberculosis* as 1 of 4 antibiotic drug–resistant pathogens of critical global priority (*1*). According to WHO's 2024 Global TB report, 400,000 persons worldwide develop tuberculosis (TB) caused by a multidrug-resistant/rifampin-resistant (MDR/RR) *M. tuberculosis* (*2*). Of note, the estimated proportion of MDR/RR TB among all new TB cases is 3.2%, whereas among previously treated cases, that figure was 16% (*2*). Regional disparities in the global burden of MDR/RR TB are profound. The greatest incidence is observed in Eastern Europe and Central Asia, where up to 20% of new TB cases and >50% of previously treated cases exhibit MDR/RR TB. Those regions face considerable challenges in implementing effective TB control measures (*2*).

WHO's 2024 recommendations for drug-resistant TB management included several short treatment regimens, which have shown high efficacy in curing MDR/RR TB. Treatment durations are 6–9 months, which are substantially shorter than the standard 18–20-month regimen (*3*). Eligibility for shorter regimens requires confirmation of drug susceptibility within the regimen. In cases where resistance to agents used in 6- and 9-month regimens is confirmed or suspected, patients must undergo the longer 18-month course. However, emerging resistance to key second-line TB treatment agents in multiple regions threatens the real-world effectiveness of those treatment approaches (*4*).

The objective of this study was to assess resistance rates to second-line TB treatment drugs in the Kharkiv region of Ukraine (2.6 million inhabitants in 2023), which is a country with a high burden of drug-resistant TB, and to compare those findings with our previously reported data from the same region (*5*). We analyzed data from phenotypic drug susceptibility testing, as recorded in the Electronic Register of the TB-Control Program in Kharkiv, for the specified period. Results indicated that 23.1%–31.2% of patients in Kharkiv affected by MDR/RR TB during 2019–2023 had additional resistance to levofloxacin at ≈3-fold greater level than the 10% observed in 2014. Similarly, resistance to moxifloxacin ranged from 10.6% to 20.9% and was the highest rate recorded in the past 2 years, suggesting a notable upward trend in fluoroquinolone resistance (Table). Conversely, resistance to other group A agents (bedaquiline and linezolid) and group B agents (clofazimine and cycloserine) remained low at <1%. We observed high levels of resistance for pyrazinamide (a drug belonging to group C on the WHO drug list), which is a component medicine in the 2024 WHO-recommended 9-month MDR TB regimens. Resistance to pyrazinamide ranged from 54.3% to 58.7% during 2019–2023, compared with 69.6% in 2014.

The substantial increase in fluoroquinolone resistance observed in this study is particularly alarming. Fluoroquinolones play a critical role in MDR/RR TB treatment. Resistance to those agents is a key criterion for defining pre–extensively drug-resistant TB. That resistance is also a noteworthy factor linked to poorer outcomes in patients with MDR/RR TB (*6*). Consequently, because up to 30% of patients in Kharkiv with MDR/RR TB are infected with *M. tuberculosis* strains exhibiting fluoroquinolone resistance, effective TB control faces considerable challenges at times of military oppression. A contributing factor to the rise in fluoroquinolone resistance is likely the insufficient availability or improper use of second-line TB medications (*7*). Our 2014 data indicated deficiencies

Table. Resistance to second-line drugs in a study of fluoroquinolone resistance in drug-resistant TB, Kharkiv, Ukraine, 2019–2023*

Category	2014	2019	2020	2021	2022	2023	Kendall τ
No. patients with MDR/RR TB	169	333	231	243	155	262	0.07
New TB patients with MDR/RR TB, no. (%)	104 (61.5)	256 (76.9)	178 (77.1)	173 (71.2)	125 (80.6)	187 (71.4)	0.07†
Group A drugs, % resistant							
Moxifloxacin	14.9	NT	15.0	10.6	20.8	20.9	0.6
Levofloxacin	10.0	23.1	27.2	26.9	31.2	28.2	0.73
Bedaquiline	NT	NT	0	0	0.7	0.4	0.55
Linezolid	2.9	0.3	0	0.5	2.7	0.4	−0.07
Group B drugs, % resistant							
Clofazimine	NT	0	0	0	0	0.4	0.63
Cycloserine	5.8	0	NT	NT	NT	NT	NA
Group C drugs, % resistant							
Ethambutol	66.3	75.4	60.1	37.9	49.4	54.4	−0.47
Delamanid	NT	0	1.8	0.9	0.7	1.7	0.2
Pyrazinamide	69.6	54.9	54.9	54.3	55.3	58.6	0
Imipenem/meropenem	NT	NT	NT	NT	NT	NT	NA
Amikacin	23.4	12.4	13.2	18.5	20.4	18.0	0.07
Streptomycin	95.9	75.3	78.4	NT	NT	NT	−0.33
Ethionamide	33.6	32.7	26.1	24.4	27.3	NT	−0.6
Para-aminosalicylic acid	3.1	NT	NT	NT	NT	NT	NA

*Results referred to phenotypic drug susceptibility testing, performed by using the BACTEC MGIT960 culture system (Becton Dickinson, https://www.bd.com), applying World Health Organization–recommended critical concentrations. Drug groups are from the World Health Organization (*3*). MDR/RR, multidrug resistant/rifampin resistant; NA, not applicable; NT, not tested; TB, tuberculosis.
†The Kendal τ coeficient for the trend for the percentage of new TB patients over the study period 2014 and 2019–2023 was 0.33.

in MDR/RR TB management at the Kharkiv TB Dispensary, suggesting that the high rates of fluoroquinolone resistance observed during 2019–2023 could be a consequence of suboptimal possibilities for the management of patients with drug-resistant TB in previous years.

In addition to their role in MDR/RR TB treatment, fluoroquinolones are frequently prescribed empirically for common bacterial infections, such as pneumonia and sinusitis. In cases where fluoroquinolones are used as monotherapy for patients with undiagnosed TB, that practice may contribute to bacillary resistance across that drug class (*8*). The resulting symptom relief can delay TB diagnosis, thereby increasing community transmission risk (*9*). In Ukraine, the unregulated use of antibiotic drugs is common practice (*10*), adding to the increase in *M. tuberculosis* resistance to fluoroquinolones. The rapid development of resistance observed here should serve as a cautionary example as new MDR/RR TB drugs, such as bedaquiline, are introduced into clinical settings. Rapid resistance development poses a potential threat to the efficacy of newly implemented TB treatment drugs such as bedaquiline, even if data from this study do not yet reflect such resistance.

In conclusion, given the ongoing military conflict in the region, heightened vigilance regarding the potential for worsening drug resistance among patients with MDR TB in Kharkiv is essential. Additional efforts to mitigate factors that may contribute to rising resistance should be prioritized to prevent further escalation of the public health threat.

D.C. and C.L. are supported by the German Center of Infection Research (grant agreement no. 02.709).

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Neurosarcocystosis in Patient with HIV-Induced Immunodeficiency

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DOI: https://doi.org/10.3203/eid3103.241361

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Sarcocystis is a genus of protozoan parasites that can infect various vertebrates. In humans, *Sarcocystis* infection usually is asymptomatic but might manifest as a mild gastroenteritis or extraintestinal myositis. We report a case of human central nervous system infection in Norway caused by *S. nesbitti* parasites.

The genus *Sarcocystis* consists of apicomplexan parasites, ≈200 species of which can infect reptiles, birds, and mammals; however, few species are zoonotic (*1*). Humans are definitive hosts of *S. hominis*, *S. suihominis*, and *S. heydorni*, shedding oocysts after ingestion of undercooked meat from intermediate hosts containing tissue cysts (*1*). Gastrointestinal infection is asymptomatic or causes a mild, self-limiting gastroenteritis (*2*). Human muscular sarcocystosis is a rare clinical syndrome associated with *S. nesbitti* infection mostly documented in Malaysia (*2*). The natural reservoirs of *S. nesbitti* parasites are probably reptiles, particularly snakes in Southeast Asia and Australia (*3*,*4*). Intermediate hosts, including humans, might develop tissue sarcocystosis after ingesting *S. nesbitti* sporocysts from fecally contaminated food or water. In Thailand, the prevalence of intestinal sarcocystosis is 7.0%–23.2% (*5*,*6*), but data regarding tissue sarcocystosis and *S. nesbitti* infection are scarce. We report a human case of *S. nesbitti* central nervous system infection in Norway.

The patient, a White male in his 70s, had lived in Norway for ≈40 years and visited Thailand for several months a year for 10 years. While in southern Thailand, he experienced increasing back pain and acute diplopia, aphasia, unilateral hemiparesis, and urinary and fecal incontinence. Imaging conducted in a clinic in Thailand revealed multiple brain lesions, and he returned to Norway for further investigations.

Upon the patient's hospital admission in Norway, initial laboratory workup revealed an undiagnosed HIV infection (viral load 50,000 copies/mL, CD4+ T-cell count 116 cells/mm^3). Magnetic resonance imaging showed numerous cortical and subcortical contrast-enhancing lesions in both cerebral hemispheres, along with multiple cerebellar, cervical, and thoracic spinal cord lesions (Figure). We noted hemorrhagic components and substantial perilesional edema (Figure). 18F-fluorodeoxyglucose (FDG) positron emission tomography–computed tomography demonstrated intense focal FDG uptake corresponding to areas of contrast enhancement found on magnetic resonance imaging. Apart from a diffusely increased signal in gluteal muscles, we noted no abnormal FDG uptake outside the central nervous system (CNS). The overall assessment suggested metastatic cancer, with opportunistic infection as a differential diagnosis.