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**境外学者发表的结核病英文文章摘要**

**（84篇）**

**PubMed Publication date: 2025/8/25 --- 2025/8/31**

**(tuberculosis[Title/Abstract]) AND (English[Language])**

**1. Clin Exp Med. 2025 Aug 31;25(1):308. doi: 10.1007/s10238-025-01797-7.**

The dual burden of tuberculosis and diabetes mellitus: an epidemiological

correlation.

Bibi S(1), Khan H(2)(3), Salman M(1), Khan J(4), Shah TA(5), Assefa M(6), Hassan

HM(7).

Author information:

(1)Department of Health and Biological Sciences, Abasyn University Peshawar,

Peshawar, Pakistan.

(2)Department of Health and Biological Sciences, Abasyn University Peshawar,

Peshawar, Pakistan. hayatbiotech@yahoo.com.

(3)University Institute of Medical Laboratory Technology, The University of

Lahore, Lahore, Pakistan. hayatbiotech@yahoo.com.

(4)Department of Allied Health Sciences, Sarhad University of Science &

Information Technology, Islamabad Campus, Islamabad, Pakistan.

jadoonkhan@bs.qau.edu.pk.

(5)College of Agriculture Engineering and Food Science, Shandong University of

Technology, Zibo, 255000, China.

(6)Southern Agricultural Research Institute, Werabe Agricultural Research

Center, P.O. Box. 21, Werabe, Ethiopia. molalensafa@gmail.com.

(7)Department of pathology, College of Medicine, King Khalid University, Abha,

Saudi Arabia.

This study examined the association between diabetes mellitus and tuberculosis

(TB) in a cohort of 200TB-positive patients, stratified by gender, age,

treatment regimen, and comorbidities, including diabetes, acute gastroenteritis,

and hypertension, compared to TB patients without additional complications.

Clinical parameters-Random Blood Sugar (RBS), C-reactive protein (CRP), and

Erythrocyte Sedimentation Rate (ESR)-were assessed at baseline and after four

months of anti-TB therapy. The results showed no significant changes in mean RBS

or CRP levels post-treatment, but a notable reduction in mean ESR was observed.

Age and gender had minimal impact on therapeutic outcomes for RBS, CRP, or ESR,

though females exhibited higher ESR values than males. Treatment regimens,

whether Myrin P Forte alone or combined with streptomycin, did not significantly

alter clinical parameters. However, CRP levels improved in TB patients with

comorbidities, such as diabetes, hypertension, or gastroenteritis. A significant

prevalence of diabetes (21.42%) was found among TB patients, with higher rates

in females and those over 50 years. These findings highlight a notable

association between diabetes and TB. However, the minimal effect of anti-TB

therapy on clinical parameters suggests that ESR and CRP may not be reliable

prognostic markers for TB. The study underscores the need for further

large-scale case-control studies and molecular research to better understand the

relationship between diabetes and TB, particularly given the high prevalence of

diabetes among TB patients.

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DOI: 10.1007/s10238-025-01797-7

PMID: 40886212 [Indexed for MEDLINE]

**2. Cell Rep. 2025 Aug 29;44(9):116184. doi: 10.1016/j.celrep.2025.116184. Online**

**ahead of print.**

CD226 identifies effector CD8(+) T cells during tuberculosis and costimulates

recognition of Mycobacterium tuberculosis-infected macrophages.

Shinkawa T(1), Chang E(2), Rakib T(2), Cavallo K(1), Lai R(1), Behar SM(3).

Author information:

(1)Department of Microbiology, University of Massachusetts Medical School,

Worcester, MA, USA.

(2)Department of Microbiology, University of Massachusetts Medical School,

Worcester, MA, USA; Immunology and Microbiology Program, Graduate School of

Biomedical Science, Worcester, MA, USA.

(3)Department of Microbiology, University of Massachusetts Medical School,

Worcester, MA, USA. Electronic address: samuel.behar@umassmed.edu.

CD8+ T cells defend against Mycobacterium tuberculosis (Mtb) infection but

variably recognize Mtb-infected macrophages. To investigate how chronic

infection affects the diversity of lung parenchymal CD8+ T cells, we perform

single-cell RNA sequencing (scRNA-seq) on cells from C57BL/6J mice infected for

6 and 41 weeks. We identify an effector lineage, including a cluster that

expresses high levels of cytotoxic effectors and cytokines, and a dysfunctional

lineage that transcriptionally resembles exhausted T cells. The most

significantly differentially expressed gene between two distinct CD8+ T cell

lineages is Cd226. Mtb-infected interferon (IFN)γ-enhanced yellow fluorescent

protein (EYFP) reporter mice reveal that IFNγ production is enriched in

CD226+CD8+ T cells, confirming these as functional T cells in vivo. Purified

CD226+ but not CD226- CD8+ T cells recognize Mtb-infected macrophages, and CD226

blockade inhibits IFNγ and granzyme B production. Thus, efficient CD8+ T cell

recognition of Mtb-infected macrophages requires CD226 costimulation, and CD226

expression identifies CD8+ T cells that recognize Mtb-infected macrophages.

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PMID: 40886314

**3. Clin J Gastroenterol. 2025 Aug 31. doi: 10.1007/s12328-025-02213-z. Online ahead of print.**

Late-onset paradoxical response 11 years after treatment of tuberculous hepatic

abscesses in an HIV-negative patient: a case report and literature review.

Suzue K(1), Tanaka Y(2), Akazawa N(1), Saito A(1), Yamamoto N(1), Akiyama JI(1),

Igari T(3), Takasaki J(4), Yanase M(1).

Author information:

(1)Department of Gastroenterology, National Center for Global Health and

Medicine, Japan Institute for Health Security, 1-21-1 Toyama, Shinjuku-Ku,

Tokyo, 162-8655, Japan.

(2)Department of Gastroenterology, National Center for Global Health and

Medicine, Japan Institute for Health Security, 1-21-1 Toyama, Shinjuku-Ku,

Tokyo, 162-8655, Japan. tanaka.y@jihs.go.jp.

(3)Department of Pathology, National Center for Global Health and Medicine,

Japan Institute for Health Security, 1-21-1 Toyama, Shinjuku-Ku, Tokyo,

162-8655, Japan.

(4)Department of Respiratory Medicine, National Center for Global Health and

Medicine, Japan Institute for Health Security, 1-21-1 Toyama, Shinjuku-Ku,

Tokyo, 162-8655, Japan.

Paradoxical responses (PRs) to anti-tuberculosis (anti-TB) treatment refer to

the worsening of pre-existing tuberculous lesions or the emergence of new

lesions in patients whose clinical symptoms initially improved with therapy. PRs

are less common in HIV-negative patients, and presentations as tuberculous

hepatic abscesses are rare. Furthermore, PRs occurring after completion of TB

treatment are uncommon, making it difficult to distinguish them from TB relapse.

We report herein a case of late-onset post-treatment PR, presenting 11 years

after completion of treatment for a tuberculous hepatic abscess in an

HIV-negative patient. A 51-year-old HIV-negative woman undergoing maintenance

hemodialysis, with a history of pulmonary TB with hepatic and splenic abscesses,

completed anti-TB treatment 11 years earlier. She was hospitalized after

multiple liver nodules were detected on computed tomography. Suspecting a

tuberculous hepatic abscess due to TB relapse or PR, we performed an

ultrasound-guided liver biopsy. Histopathological analysis revealed epithelioid

granulomas with caseous necrosis. However, both polymerase chain reaction and

culture for TB were negative. She was therefore diagnosed with late-onset

post-treatment PR and carefully observed without treatment. The liver abscesses

eventually regressed spontaneously. This case highlights the importance of

considering PRs even long after TB treatment completion and underscores the need

to avoid unnecessary administration of anti-TB drugs.

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Gastroenterology.

DOI: 10.1007/s12328-025-02213-z

PMID: 40886220

**4. Lancet. 2025 Aug 30;406(10506):908-909. doi: 10.1016/S0140-6736(25)01664-2.**

Why are we failing to rapidly diagnose tuberculosis in the UK?

Drobniewski F(1), Kon OM(2), Gonzalo X(3), Ashmi M(4).

Author information:

(1)Imperial College London, London SW7 2AZ, UK. Electronic address:

f.drobniewski@imperial.ac.uk.

(2)Imperial College Healthcare NHS Trust, London, UK.

(3)Barts Health NHS Trust, London, UK.

(4)Imperial College London, London SW7 2AZ, UK.

DOI: 10.1016/S0140-6736(25)01664-2

PMID: 40885573

**5. Arch Microbiol. 2025 Aug 30;207(10):245. doi: 10.1007/s00203-025-04415-y.**

Recent advancements in drug development for pulmonary tuberculosis.

Mukherjee K(1), Saha P(2), Ganguly KK(3), Chakraborty S(4), Ghosh S(4), Kundu

G(4).

Author information:

(1)Department of Microbiology, Kalyani Mahavidyalaya, City Centre Complex,

Kalyani, Nadia, West Bengal, 741235, India. koushikmukh@gmail.com.

(2)Department of Chemistry, Kalyani Mahavidyalaya, City Centre Complex, Kalyani,

Nadia, West Bengal, 741235, India.

(3)Department of Microbiology, Michael Madhusudan Memorial College, Durgapur,

West Bengal, 713216, India.

(4)Department of Microbiology, Kalyani Mahavidyalaya, City Centre Complex,

Kalyani, Nadia, West Bengal, 741235, India.

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), is a global

health threat. Despite advances in diagnostics and treatment regimens, it

infects millions annually. It remains a significant global health challenge,

particularly due to the appearance of resistance towards anti-tuberculosis drugs

(ATD), mainly multidrug-resistant (MDR) and extensively drug-resistant (XDR)

strains. Mtb poses resistance towards the currently used first- and second-line

regimen. Recent advancements in drug development have introduced therapeutic

options focussed on improving treatment outcomes for both drug-sensitive and

drug-resistant TB. This includes the implementation of a shorter 6-month

regimen, a combination of bedaquiline, pretomanid, linezolid, and moxifloxacin

(BPaLM), and all-oral treatment regimens (nine months treatment) for patients

with MDR/Rifampicin TB-resistance. Another longer 18-20-month regimen is also

accessible for patients with TB resistance, for whom all other regimens or

treatments are not feasible due to various factors. Ongoing research into new

drug molecules, adjunct therapies, and advancement in faster diagnosis aims to

enhance the efficacy and tolerability of TB treatment while tackling challenges

related to adherence and resistance. This review will discuss the limitations of

current treatment regimens, and recent developments in the pharmacological

landscape of TB management, highlighting innovative strategies and the necessity

for continued efforts to combat the evolving threat of this headstrong pathogen.

The findings underscore the importance of a patient-centered approach in TB

treatment to achieve equitable and sustainable health outcomes globally.

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part of Springer Nature.

DOI: 10.1007/s00203-025-04415-y

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**6. J Infect Dis. 2025 Aug 30:jiaf456. doi: 10.1093/infdis/jiaf456. Online ahead of print.**

c-Myc inhibits macrophage antimycobacterial response in Mycobacterium

tuberculosis infection.

Sarti E(1), Dollé C(1), Wolfensberger R(1), Kusejko K(1)(2), Russenberger D(1),

Bredl S(1), Speck RF(1), Greter M(3), Rueschoff JH(4), Boeck L(5), Mai D(6),

Jahn AN(6), Gold ES(6), Liu D(6), Diercks AH(6), Sander P(7)(8), Olson GS(5)(9),

Nemeth J(1).

Author information:

(1)Department of Infectious Diseases and Hospital Epidemiology, University

Hospital Zurich, University of Zurich, 8091 Zurich, Switzerland.

(2)Institute of Medical Virology, University of Zurich, 8057 Zurich,

Switzerland.

(3)Institute of Experimental Immunology, University of Zurich, 8057 Zurich,

Switzerland.

(4)Department of Pathology and Molecular Pathology, University Hospital Zurich,

8091 Zurich, Switzerland.

(5)Department of Biomedicine, University of Basel, 4031 Basel, Switzerland.

(6)Center for Global Infectious Disease Research, Seattle Children's Research

Institute, Seattle, WA 98109, United States of America.

(7)Institute of Medical Microbiology, University of Zurich, 8006 Zurich,

Switzerland.

(8)National Reference Laboratory for Mycobacteria, University of Zurich, 8006

Zurich, Switzerland.

(9)Department of Laboratory Medicine and Pathology, University of Washington,

Seattle, WA 98115, United States of America.

Mycobacterium tuberculosis (MTB) remains a major cause of global mortality, yet

natural immunity prevents disease in more than 90% of exposed individuals.

Interferon gamma (IFN-γ) is a critical regulator of innate immunity and enhances

macrophage antimicrobial responses. In this study, we investigated how IFN-γ

timing influences macrophage control of MTB. We found that pre-infection IFN-γ

exposure primes macrophages for enhanced bacterial control by activating key

antimicrobial pathways, whereas post-infection exposure fails to confer this

benefit. Using unbiased in vitro systems approaches, we identified c-Myc

signaling as a central determinant of macrophage antimycobacterial function. To

manipulate c-Myc in primary cells, we developed a tetracycline-inducible

lentiviral system for c-Myc inhibition and overexpression. c-Myc inhibition via

Omomyc enhanced macrophage bacterial control through mTORC1-dependent metabolic

reprogramming and nitric oxide production. In vivo analyses, including murine

models and human clinical histopathology, revealed strong associations between

c-Myc expression, MTB persistence, and active tuberculosis, implicating c-Myc as

a mediator of immune privilege in MTB infection and a promising target for

host-directed therapies to enhance macrophage function.

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Infectious Diseases Society of America.

DOI: 10.1093/infdis/jiaf456

PMID: 40884499

**7. Int J Tuberc Lung Dis. 2025 Aug 29;29(9):416-421. doi: 10.5588/ijtld.25.0055.**

Implementing TB preventive therapy: lessons from a large-scale initiative in

India.

Das M(1), Kalra A(1), ThekkePurakkal AS(1), Showket T(1), Raj S(1), Panibatla

V(2), Imran D(3), Solanki H(4), Taralekar R(4), Rao R(5), Dhawan V(5), Parmar

M(6), Yassin M(7), Chadha SS(8), Sarin S(8), Singh U(5).

Author information:

(1)FIND, New Delhi, India.

(2)TB Alert India, Telangana, India.

(3)Karnataka Health Promotion Trust, Karnataka, India.

(4)Central TB Division, WHO NTEP Technical Support Network, New Delhi, India.

(5)Central TB Division, Ministry of Health and Family Welfare, New Delhi, India.

(6)World Health Organization, Country Office for India, New Delhi, India.

(7)The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland.

(8)FIND, Geneva, Switzerland.

**BACKGROUND** TB infection management is essential in addressing

the global TB burden. TB programmes worldwide are focusing on WHO-recommended

shorter duration TB preventive treatment (TPT). We document early findings of

3HP regimen (rifapentine-isoniazid weekly doses for 3 months) implementation

under the Joint Effort for Elimination of Tuberculosis (JEET) project in

India. **METHODS** his is a descriptive cohort study involving household contacts (HHCs) of pulmonary TB patients on TPT in select districts of the JEET project supported by FIND. The HHCs received 3HP in two districts while those in other districts received 6-month daily isoniazid (6H) during April-September 2022. The study compared characteristics, adverse events (AEs) and TPT outcomes of HHCs on 3HP with those on 6H. **RESULTS** A total of 635 HHCs were initiated on 3HP,

while 24,350 HHCs received 6H. About 10% of HHCs on 3HP developed AEs compared

with 4% HHCs on 6H. However, a higher proportion of HHCs on 3HP completed TPT

compared with HHCs on 6H (95% vs. 84%, P < 0.001). **CONCLUSION** High TPT completion rates for 3HP with low levels of manageable AEs support expansion of 3HP under national TB programmes. The 3HP TPT regimen could be considered an effective shorter TPT option in high-TB-burden countries.</sec>.

DOI: 10.5588/ijtld.25.0055

PMID: 40883881 [Indexed for MEDLINE]

**8. Dev Biol. 2025 Aug 27:S0012-1606(25)00236-2. doi: 10.1016/j.ydbio.2025.08.019.**

**Online ahead of print.**

Unusually High Prevalence of Cervical Ribs in an 18th-Century Hungarian Town:

The Impact of a Tuberculosis Epidemic.

Galis F(1), van der Geer AAE(2), Van Dooren TJM(3), Szeniczey T(4), Hajdu T(5),

Kiss K(6), Pap I(7).

Author information:

(1)Institute of Biology, Leiden University, Leiden, The Netherlands; Naturalis

Biodiversity Center, Leiden University, Leiden, The Netherlands. Electronic

address: frietson.galis@naturalis.nl.

(2)Institute of Biology, Leiden University, Leiden, The Netherlands; Naturalis

Biodiversity Center, Leiden University, Leiden, The Netherlands. Electronic

address: Alexandra.vandergeer@naturalis.nl.

(3)Naturalis Biodiversity Center, Leiden University, Leiden, The Netherlands;

CNRS, Institute of Ecology and Environmental Sciences (IEES Paris), Sorbonne

University, Paris, France. Electronic address: tvdooren@gmail.com.

(4)Department of Biological Anthropology, Eötvös Loránd University, Budapest,

Hungary. Electronic address: tamas.szeniczey@ttk.elte.hu.

(5)Department of Biological Anthropology, Eötvös Loránd University, Budapest,

Hungary. Electronic address: tamas.hajdu@ttk.elte.hu.

(6)Institute of Practical Methodology and Diagnostics, Faculty of Health

Sciences, University of Miskolc, Miskolc, Hungary; Department of Biological

Anthropology, Eötvös Loránd University, Budapest, Hungary; HUN-REN Research

Centre for the Humanities, Institute of Archaeogenomics, Tóth Kálman utca 4,

Budapest. Electronic address: krisztian.kiss@ttk.elte.hu.

(7)Department of Biological Anthropology, Eötvös Loránd University, Budapest,

Hungary; Department of Biological Anthropology, University of Szeged, Hungary.

Electronic address: ildiko.pap.2@hotmail.com.

Tuberculosis (TB) ravaged the Hungarian town of Vác in the 18th century. Nearly

all of the young and middle-aged adults buried in the Dominican Church were

infected with TB. Therefore, most women were likely infected with Mycobacterium

tuberculosis (MTB) during pregnancy. In rodents, disruptions in early gestation,

when the head-to-tail patterning of the embryo occurs, often result in an

increased incidence of cervical ribs. Because TB severely disrupts pregnancy, we

hypothesized that these disruptions would result in an increased number of

cervical ribs in Vác residents. We examined 58 skeletons and found, as

predicted, that the incidence of cervical ribs is exceptionally high in this

population. Cervical ribs are approximately twenty-five times more common than

in the healthy general population and shifts of the thoracolumbar boundary two

to five times more common. Cervical ribs are usually associated with other

congenital anomalies, including other homeotic vertebral transformations.

Homeotic transformations at different vertebral boundaries were usually in the

same direction and sometimes involved three boundaries. This implies a prolonged

disruption of pregnancy and alterations in multiple Hox gene expression domains.

Our study emphasizes that a high incidence of cervical ribs indicates

vulnerability. Our data support the idea that cervical ribs can be induced not

only by genetic changes, but also by infectious diseases and thus by

environmental perturbations of pregnancy.

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PMID: 40882913

**9. Anal Sci Adv. 2025 Aug 26;6(2):e70034. doi: 10.1002/ansa.70034. eCollection 2025 Dec.**

Computational Framework for High Copy-Number Probe Selection and Cross-Binding

Reduction.

Kim Y(1), Mohanty SK(1)(2).

Author information:

(1)Department of Materials Science and Engineering The University of Utah Salt

Lake City Utah USA.

(2)Department of Chemical Engineering The University of Utah Salt Lake City Utah

USA.

DNA probe design plays a critical role in biosensor-based disease diagnostics,

gene expression analysis and environmental monitoring. Traditional probe designs

primarily target lower-copy genetic sequences, often leading to low detection

sensitivity due to limited hybridization events. This study introduces a novel

probe design strategy that leverages highly repetitive DNA sequences as target

sites to amplify biosensor signals without requiring PCR-based amplification.

The computational selection process is conducted using a custom-developed

bioinformatics tool to identify repetitive sequences across the entire

Mycobacterium tuberculosis genome, independent of gene boundaries. The

identified sequences are then cross-referenced against the Homo sapiens genome

using BLAST to minimize host cross-reactivity. The analysis revealed that a

23 bp sequence repeated 39 times in M. tuberculosis exhibits only 78% sequence

identity with human DNA and is present in just two copies within the human

genome. This suggests that the selected probe may yield substantially stronger

hybridization signals for M. tuberculosis relative to human cfDNA, thereby

enhancing biosensor sensitivity. The computational methodology introduced in

this study provides a robust framework for designing high-sensitivity

biosensors, enabling more effective infectious disease diagnostics,

environmental monitoring and clinical point-of-care testing.

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**10. BMC Infect Dis. 2025 Aug 28;25(1):1078. doi: 10.1186/s12879-025-11497-y.**

Non-tuberculous mycobacterial infections among pulmonary tuberculosis suspected

and confirmed patients in Ethiopia - A systematic review and meta analyses.

Daka D(1)(2), Tessema B(3)(4), Mutshembele A(5), Alelign A(3), Birhan W(3),

Gelaw B(3).

Author information:

(1)Hawassa University college of Medicine and health sciences, Hawassa,

Ethiopia. drsdk200@gmail.com.

(2)College of Medicine and Health sciences, Department of Medical Microbiology,

Univeristy of Gondar, Gondar, Ethiopia. drsdk200@gmail.com.

(3)College of Medicine and Health sciences, Department of Medical Microbiology,

Univeristy of Gondar, Gondar, Ethiopia.

(4)Institute of Clinical Immunology, Faculty of Medicine, University of Leipzig,

Leipzig, Germany.

(5)South African Medical Research Council, South Africa Office of AIDS and TB,

Pretoria, South Africa.

**INTRODUCTION:** Nontuberculous mycobacteria (NTM) are environmental pathogens

found in soil, water, and various environments, causing chronic pulmonary

infections. They are resistant to chlorine and extreme temperatures but not

typically transmissible. NTM infections are often misdiagnosed as tuberculosis

(TB), especially in Ethiopia, where data on prevalence is scarce. This research

aims to analyze NTM isolation from pulmonary samples and other specimens used in

pulmonary tuberculosis (PTB) diagnosis among patients suspected or confirmed as

PTB cases in Ethiopia.

**OBJECTIVE:** This study systematically reviews and synthesizes published studies

that report NTM isolation from sputum and other clinical samples in Ethiopia to

estimate the overall prevalence of NTM isolation, identify the common species,

and analyze regional variations in their occurrence.

**METHODS:** This systematic review and meta-analysis aimed to determine NTM

prevalence in infected individuals in Ethiopia. Using PubMed, Scopus, Web of

Science, Google Scholar, and African Journals Online, we conducted a

comprehensive literature search. Data extraction and quality assessment used the

Newcastle-Ottawa Scale. Meta-analysis employed STATA-18 software with a

random-effects model and included subgroup analysis. PROSPER registration:

CRD420251000131.

**RESULTS:** In this review a total of 5,415 participants were involved and 53.8%

were TB suspected patients, 37.6% were PTB patients, 4.0% were Multidrug

resistance-tuberculosis (MDR-TB) patients, and 4.6% were Human Immunodeficiency

virus (HIV) positive. The NTM prevalence was 3.8%, showing high heterogeneity

and regional species variability. The meta-analysis highlighted differences in

NTM prevalence across age groups and diagnostic tools, emphasizing the need for

enhanced diagnostics and continuous surveillance to improve patient outcomes and

inform public health strategies.

**CONCLUSION:** The review summarizes the epidemiology and geographical distribution

of NTM infections and common NTM species isolated among PTB suspected patients

in Ethiopia, revealing regional variations and clinical implications. Despite

limited data, Ethiopia has a lower prevalence of NTM compared to other African

regions and the worldwide average.

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PMCID: PMC12392611

PMID: 40877844 [Indexed for MEDLINE]

**11. BMC Infect Dis. 2025 Aug 26;25(1):1070. doi: 10.1186/s12879-025-11303-9.**

A comprehensive analysis of fractional-order model of tuberculosis with

treatment intervention.

Agbata BC(1), Dervishi R(2), Agbebaku DF(3), Cenaj E(2), Collins OC(3),

Ezeafulukwe AU(3), Shior MM(4), Mbah GCE(3).

Author information:

(1)Department of Mathematics and Statistics, Faculty of Science, Confluence

University of Science and Technology, Osara, Nigeria.

agbatacelestine92@gmail.com.

(2)Department of Mathematical Engineering, Mathematical and Physical Engineering

Faculty, Polytechnic University of Tirana, Tirana, Albania.

(3)Department of Mathematics, Faculty of Physical Sciences, University of

Nigeria, Nsukka, Nigeria.

(4)Department of Mathematics/Computer Science, Benue State University, Makurdi,

Nigeria.

Tuberculosis (TB) remains one of the top infectious disease killers worldwide,

with an estimated 10.6 million new cases and 1.3 million deaths reported in 2022

alone (WHO, 2023). The COVID-19 pandemic has further disrupted TB control

efforts by limiting access to healthcare services, interrupting treatment

regimens, and delaying diagnoses and leading to a resurgence in TB transmission.

Tuberculosis is caused by Mycobacterium tuberculosis and spread through the air,

TB posing a serious threat to vulnerable populations, especially those with

weakened immune systems such as individuals living with HIV. These challenges

emphasize the need for more robust and realistic modeling approaches to inform

policy and intervention. In this study, We incorporated fractional-order

derivatives and applied the Adams-Bashforth method to better understand how TB

spreads and how it can be controlled. The model divides the population into six

key groups: those susceptible to infection, exposed individuals, people with

acute TB, those with chronic TB, individuals undergoing treatment, and those who

have recovered. To capture the complexities of TB transmission, we incorporated

fractional-order derivatives along with the Adams-Bashforth method, allowing us

to account for memory effects and more accurately reflect real-world dynamics.

Sensitivity analysis revealed that increasing treatment rates significantly

improves recovery outcomes. In addition, we conducted a quantitative analysis of

the model, deriving the basic reproduction number (R₀) using the next-generation

matrix method. The results show that the endemic equilibrium is globally and

asymptotically stable when R₀ > 1, indicating that TB will persist in the

population under these conditions. Conversely, when R₀ < 1, the disease will die

out over time, highlighting the critical role of reducing transmission and

increasing treatment to achieve effective TB control. The simulations also

explored various intervention strategies, including improved treatment access,

faster diagnosis, and recognition of nonlinear transmission dynamicsThese

results emphsize the importance of timely intervention and provide actionable

insights for strengthening TB control policies.

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DOI: 10.1186/s12879-025-11303-9

PMCID: PMC12379497

PMID: 40859186 [Indexed for MEDLINE]

**12. Indian J Pediatr. 2025 Aug 29. doi: 10.1007/s12098-025-05752-y. Online ahead of print.**

Spine Tuberculosis Presenting as Subacute-Onset Spastic Paraparesis with Upper

Back Pain.

Gupta J(1), Tiwari R(2), Gupta A(3), Mishra V(4), Meena HM(4), Sehra RN(4),

Devpura K(4), Meena K(4).

Author information:

(1)Department of Pediatrics, SMS Medical College, Jaipur, Rajasthan, India.

juhiguptadr@gmail.com.

(2)Department of Pediatrics, Medanta Hospital, Lucknow, Uttar Pradesh, India.

(3)Department of Radio-diagnosis, SMS Medical College, Jaipur, Rajasthan, India.

(4)Department of Pediatrics, SMS Medical College, Jaipur, Rajasthan, India.

DOI: 10.1007/s12098-025-05752-y

PMID: 40880045

**13. Mol Divers. 2025 Aug 29. doi: 10.1007/s11030-025-11332-1. Online ahead of print.**

Mechanistic inhibition of FtsZ-driven bacterial cytokinesis by natural products:

an integrated machine learning and advanced drug discovery approach.

Singh R(1), Tripathi V(2), Dwivedi VD(3)(4), Chouhan G(5).

Author information:

(1)Department of Biotechnology, School of Bioscience and Technology, Sharda

University, Greater Noida, 201310, India.

(2)School of Biotechnology, Gautam Buddha University, Greater Noida, India.

(3)Center for Global Health Research, Saveetha Institute of Medical and

Technical Sciences, Saveetha Medical College and Hospitals, Saveetha University,

Chennai, India.

(4)Quanta Calculus, Bioinformatics Research Division, Greater Noida, India.

(5)Department of Biotechnology, School of Bioscience and Technology, Sharda

University, Greater Noida, 201310, India. garimachouhan68@gmail.com.

Tuberculosis (TB), caused by Mycobacterium tuberculosis (MTB), remains a major

global health burden, particularly due to the emergence of multidrug-resistant

(MDR) and extensively drug-resistant (XDR) strains. The FtsZ protein, essential

for bacterial cytokinesis and lacking a human homolog, presents a selective and

non-redundant drug target. In this study, we implemented a comprehensive

computational pipeline to identify potential FtsZ inhibitors from the COCONUT

natural product database. Initial high-throughput virtual screening and machine

learning-based pIC50 prediction were employed to shortlist active compounds. The

top candidates were further optimized using Density Functional Theory, followed

by ADMET screening, redocking, and 1000-ns molecular dynamics simulations.

Binding free energy estimation via MM/GBSA identified CNP0281420

(-53.40 ± 5.57 kcal/mol), CNP0277831 (-50.06 ± 4.19 kcal/mol), and CNP0310586

(-49.47 ± 3.73 kcal/mol) as top binders. These results were supported by QM/MM

total energy calculations and PCA-based Free Energy Landscape (FEL) mapping,

confirming their conformational stability and electronic compatibility with the

FtsZ binding pocket. Overall, this integrative study highlights promising

natural compounds with strong binding affinity and dynamic stability,

positioning them as potential anti-TB drug candidates for future experimental

validation.

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AG.

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**14. Indian J Gastroenterol. 2025 Aug 29. doi: 10.1007/s12664-025-01860-x. Online**

**ahead of print.**

Child-Turcotte-Pugh score-based modified anti-tubercular treatment in patients

with decompensated cirrhosis with tuberculosis: A two-year retrospective

observational study from North India.

Ahmad J(1).

Author information:

(1)Myra Liver Gastro and Endoscopy Centre, Chowk, Lucknow, 226 020, India.

ahmadjuned43.jk@gmail.com.

**BACKGROUND:** Management of tuberculosis in decompensated cirrhosis is

challenging, as the risk of severe liver failure is markedly increased if

hepatotoxicity develops secondary to anti-tubercular treatment (ATT).

Child-Turcotte-Pugh (CTP) score-based ATT by Dhiman et al. proposed that the

number of hepatotoxic drugs should be two, one and none in CTP scores of ≤ 7,

8-10 and ≥ 11, respectively. We present here our retrospective observational

study of treating tuberculosis in patients with decompensated cirrhosis

utilizing the above-mentioned CTP-based ATT regimens.

**METHODS:** A retrospective observational study utilizing electronic data search

was conducted on the application-based software for the duration from April 2022

to April 2024. On the software, decompensated cirrhosis with tuberculosis

patients were already tagged. The modified ATT regimens (weight-based) were as

per the CTP score. With CTP score ≥ 11, no hepatotoxic drug was included:

Intensive Phase -ELA (Ethambutol, Levofloxacin and Amikacin); Continuation

Phase: EL. With CTP scores 8-10, 1 hepatotoxic drug (rifampicin preferred) was

included; Intensive Phase: RELA, R Rifampicin; Continuation Phase: REL. CTP

score ≤ 7 received two hepatotoxic drugs, Intensive Phase: HREL, H Isoniazid,

Continuation Phase: HRE. The duration of ATT's continuation phase was

12-18 months.

**RESULTS:** Of 155 patients with decompensated cirrhosis, 21 (13.5%) had

concomitant tuberculosis. CTP score-based modified ATT was administered to all

21 during the Intensive phase. Drug-induced hepatotoxicity developed in four

patients (19.1%) during the intensive phase. After the intensive phase, two

patients were lost to follow-up. Out of 19 patients who completed the

continuation phase, 15 (78.9%) had a resolution of tuberculosis and four (21.1%)

died. The cause for death in all four patients was related to cirrhosis.

**CONCLUSION:** As per our study, patients with decompensated cirrhosis tolerated

the CTP-score-based modified ATT and almost 80% had a resolution of

tuberculosis.

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**15. Neurol Sci. 2025 Aug 29. doi: 10.1007/s10072-025-08410-5. Online ahead of print.**

Circulating MicroRNAs as diagnostic indicators in tuberculous Meningitis-A case

-control study in North Indian population.

Ritika(1), Singh V(2), Singh VK(3), Nath Chaurasia R(1), Pathak A(1), Joshi

D(1), Kumar A(1), Mishra VN(1).

Author information:

(1)Department of Neurology, Institute of Medical Sciences, Banaras Hindu

University, Varanasi, 221005, Uttar Pradesh, India.

(2)Department of Geriatrics, Institute of Medical Sciences, Banaras Hindu

University, Varanasi, 221005, Uttar Pradesh, India.

(3)Department of Neurology, Institute of Medical Sciences, Banaras Hindu

University, Varanasi, 221005, Uttar Pradesh, India. mailurvarun@gmail.com.

**PURPOSE:** Tuberculous meningitis (TBM), a severe and often fatal form of

tuberculosis, showing high mortality and long-term neurological sequelae. Recent

evidence suggests that microRNAs play a crucial role in TBM pathogenesis and may

serve as potential biomarkers for diagnosis and disease progression.

**METHODS:** Eight TBM patients and three healthy controls were recruited. Whole

blood samples RNA was extracted and processed. Sequencing was performed on the

Illumina platform with a 50-bp single-end read configuration. Data preprocessing

included quality control (FastQC), adapter trimming (Cutadapt), and alignment to

the human genome (GRCh38) using mirDeep2. Differentially expressed miRNAs were

identified using the edgeR package in R, applying a log₂ fold change threshold

of ± 1 and a false discovery rate (FDR) ≤ 0.05. Experimentally validated

miRNA-mRNA interactions were retrieved from miRTarBase, TarBase, and miRecords.

Functional enrichment and pathway analyses were conducted using clusterProfiler

and KEGG database resources in R.

**RESULTS:** hsa-miR-23b-5p and hsa-miR-27a-5p were significantly upregulated, while

hsa-miR-126-5p and hsa-miR-339-5p were downregulated in TBM. Stage-specific

miRNA expression patterns were observed, with hsa-let-7f-5p and hsa-miR-16-5p

showing significant upregulation in Stage 2 TBM compared to Stage 1. Functional

annotation of validated targets highlighted enrichment in biological processes

such as cell cycle regulation, RNA splicing, and ubiquitin-mediated proteolysis,

along with key pathways including autophagy and endocytosis, known to be

involved in mycobacterial survival and host immune response.

**CONCLUSION:** The identified differentially expressed miRNAs could serve as

biomarkers for early diagnosis and disease monitoring. Further large-scale

validation are warranted to translate these findings into clinical applications.

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**16. ChemMedChem. 2025 Aug 29:e202500085. doi: 10.1002/cmdc.202500085. Online ahead of print.**

Investigating the Mechanism of Antimycobacterial and Antiproliferative Activity

of (E)-N'-Benzylidenepyrazine-2-Carbohydrazides and their Derivatives.

Houngbedji PA(1), Nawrot DE(1), Janďourek O(1), Konečná K(1), Novák M(2),

Paterová P(3), Bárta P(1), Rambaher MH(4), Novotná E(1), Castellano C(5), Mori

M(6), Meneghetti F(6), Záhorszká M(7), Korduláková J(7), Zitko J(1).

Author information:

(1)Faculty of Pharmacy in Hradec Králové, Charles University, Ak. Heyrovského

1203, 500 03, Hradec Králové, Czech Republic.

(2)Biomedical Research Centre, University Hospital Hradec Králové, Sokolská 581,

500 05, Hradec Králové, Czech Republic.

(3)Department of Clinical Microbiology, University Hospital Hradec Králové,

Sokolská 581, 500 05, Hradec Králové, Czech Republic.

(4)Faculty of Pharmacy, University of Ljubljana, Aškerčeva cesta 7, SI-1000,

Ljubljana, Slovenia.

(5)Department of Chemistry, University of Milan, Via Golgi 19, 20133, Milan,

Italy.

(6)Department of Pharmaceutical Sciences, University of Milan, Via Mangiagalli

25, 20133, Milan, Italy.

(7)Department of Biochemistry, Faculty of Natural Sciences, Comenius University

in Bratislava, Mlynská dolina, Ilkovičova 6, 842 15, Bratislava, Slovakia.

A series of 33 (E)-N'-benzylidenepyrazine-2-carbohydrazides and their

derivatives were synthesized and tested for biological activity. Benzylidene

derivatives with 2-OH substitution on the phenyl ring (18: R = 2-OH, 21:

R = 2,3-diOH, and 22: R = 2,4-diOH) exhibit various biological activities.

Compounds 18 and 21 demonstrate antimycobacterial activity against Mycobacterium

tuberculosis H37Ra, M. tuberculosis H37Rv, and M. aurum, with minimum inhibitory

concentration values ranging from 15.625 to 62.5 μg mL-1. Compounds 18, 21, and

22 show mild cytotoxicity on several human cell lines (IC50 ranging from 70.2 to

500 μM). Crystallographic studies confirm the (E)-configuration of compound 18

and a nearly planar molecular conformation. Due to their structural similarity

with salicylaldehyde isonicotinoyl hydrazone (SIH), a known iron chelator,

selected compounds were tested for iron-chelating properties, revealing

comparable or superior activity. Mechanistic assays targeting enoyl-[acyl

carrier protein] reductase (InhA), isocitrate lyase (ICL), and lipid/mycolic

acid biosynthesis show no significant inhibition, suggesting a nonspecific

mechanism potentially linked to iron chelation. A correlation is observed

between chelating activity and cytotoxicity, while antimycobacterial activity

appears to involve additional mechanisms. Pharmacokinetic studies with compound

18 reveal no specific plasma metabolites, and no significant metabolites are

detected after incubation with human liver microsomes.

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**17. J Clin Microbiol. 2025 Aug 29:e0055225. doi: 10.1128/jcm.00552-25. Online ahead of print.**

Optimization of a molecularly defined tuberculin formulation: recombinant fusion

proteins and epitope surgery.

Middleton S(1), Singh M(2), Coad M(1), Palmer S(1), Holder T(1), Steinbach S(1),

Hardiman R(1), Vordermeier HM(#)(1), Jones GJ(#)(1).

Author information:

(1)Department of Bacteriology, Animal and Plant Health Agency, Addlestone,

United Kingdom.

(2)Lionex Diagnostics and Therapeutics GmH, Braunschweig, Germany.

(#)Contributed equally

Bovine tuberculosis is an infectious livestock disease of global economic and

zoonotic importance. Surveillance programs are largely dependent on the skin

test that utilizes purified protein derivatives (PPDs) of tuberculin. PPDs

suffer from a number of limitations regarding their production,

characterization, and performance. Recently, we developed a molecularly defined

tuberculin (MDT) that overcame these limitations. The MDT formulation comprises

eight antigens, initially presented as seven recombinant proteins (ESAT6, CFP10,

Rv3615c, Rv3020c, Rv1789, Rv3478, and Rv3810) and one 20-synthetic peptide pool

representing Rv3616c; the recombinant Rv3616c could not be produced. In this

paper, we describe the steps taken to simplify the MDT formulation. First, seven

of the eight proteins were formulated as three recombinant fusion proteins.

Second, the non-immunogenic regions of Rv3616c were identified, using

overlapping peptides to probe T-cells from infected cattle. A novel variant,

Rv3616c-S4, was designed and then formulated (i) as a stand-alone protein in the

MDT-S4 formulation and (ii) fused to Rv1789 for use in the MDT-F formulation.

These novel MDT formulations gave comparable signal strength to PPD-B in

experimentally infected animals. The MDT-F, comprising only fusion proteins,

performed as well as the comparative cervical tuberculin skin test, in terms of

relative sensitivity (>2 mm; 96%, 95% CI 80-100, n = 24) and specificity (>2 mm;

100%, 95% CI 89%-100%, n = 30). In conclusion, we have developed a novel,

simplified MDT formulation that has significantly advanced our efforts toward

licensure and which has the potential to replace the PPDs developed in the

1930s.

**IMPORTANCE:** Bovine tuberculosis is an infectious livestock disease of global

economic and zoonotic importance. Surveillance programs are largely dependent on

the skin test, which utilizes tuberculins. These are crude protein extracts of

live bacterial cultures, which suffer from a number of limitations regarding

their characterization, standardization, production, and performance. We aim to

develop a skin test reagent composed of eight defined antigens that could

replace the tuberculins. This study describes the refinement of this

"molecularly defined tuberculin" (MDT) reagent into a fusion protein formulation

comprising all eight antigens. The MDT is well defined, easily standardized, and

delivers good test performance in experimentally infected, non-infected cattle

and cattle sensitized to Johne's disease. The fusion protein formulation is an

important step on the developmental pathway to a registered and marketable

product.

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**18. Microbiol Spectr. 2025 Aug 29:e0096925. doi: 10.1128/spectrum.00969-25. Online ahead of print.**

Contamination rates in serially sampled sputum specimens obtained during

tuberculosis treatment to capture culture conversion.

Niemand N(#)(1), Rooney JA(#)(2), Malatesta S(3), Rawoot N(1), Bouton TC(4),

Ragan EJ(4), Carney T(5)(6)(7), White LF(3), Farhat M(8), Horsburgh CR(4)(9),

Myers B(5)(6)(10)(11), Warren RM(1), Jacobson KR(4).

Author information:

(1)South African Medical Research Council Centre for Tuberculosis Research,

Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health

Sciences, Stellenbosch University, Cape Town, South Africa.

(2)Department of Environmental Health, Harvard T H Chan School of Public Health,

Boston, Massachusetts, USA.

(3)Department of Biostatistics, Boston University School of Public Health,

Boston, Massachusetts, USA.

(4)Department of Medicine, Section of Infectious Diseases, Boston University

Chobanian & Avedisian School of Medicine, Boston, Massachusetts, USA.

(5)Mental Health, Alcohol, Substance Use and Tobacco Research Unit, South

African Medical Research Council, Tygerberg, South Africa.

(6)Department of Psychiatry and Mental Health, University of Cape Town, Groote

Schuur Hospital, Observatory, Cape Town, South Africa.

(7)Department of Psychology, University of Johannesburg, Johannesburg, South

Africa.

(8)Department of Biomedical Informatics, Harvard Medical School, Boston,

Massachusetts, USA.

(9)Department of Epidemiology, Biostatistics and Global Health, Boston

University School of Public Health, Boston, Massachusetts, USA.

(10)Curtin enAble Institute, Faculty of Health Sciences, Curtin University,

Perth, Western Australia, Australia.

(11)West Australian Country Health Service (WACHS)-Curtin University Research

and Innovation Alliance, Curtin University, Perth, Western Australia, Australia.

(#)Contributed equally

Sputum cultures are the gold standard for tuberculosis (TB) diagnosis and

treatment monitoring. However, cultures in MGIT liquid media are susceptible to

microbial contamination, often rendering them uninterpretable. Research has

shown that maintaining strict cold chains and supervised sample collection can

reduce contamination rates, but few longitudinal studies with weekly sampling

have explored this. Here, we evaluated whether (i) the time between specimen

collection and laboratory processing and (ii) unsupervised specimen collection

are associated with contamination rates. Additionally, we estimated

contamination rates over the first 12 weeks of treatment and assessed the

clinical and behavioral predictors of contamination. We collected 3,155 sputum

specimens from 301 participants undergoing TB treatment. Contamination was

lowest (12.3%) at treatment initiation, increased over the first few weeks, and

stabilized around 30% from week 8 onwards. Samples collected without supervision

were more likely to be contaminated at treatment initiation (P = 0.048) and over

12 weeks (P = 0.028). We observed an inverse relationship between smear grade

and contamination risk throughout the sampling period. These findings underscore

the importance of supervised sputum collection to reduce contamination and

provide ways to enhance the clinical and research values of weekly cultures,

particularly those collected later in treatment. This is especially relevant for

community-collected specimens used in monitoring treatment response.IMPORTANCEIt

is essential to understand how we can minimize sputum specimen contamination

rates, as culture contamination may lead to false negative or indeterminate

results that require repeat sampling and testing, increasing the burden on

healthcare systems and potentially delaying treatment initiation. This research

underscores the importance of maintaining a stringent cold chain and highlights

the need for participant education and supervision during sample collection. The

findings from this study have important implications for TB diagnosis and

treatment outcome programs in low- and middle-income countries where biosafety

level 3 facilities are located within centralized national reference

laboratories or tertiary care hospitals.

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PMID: 40879468

**19. J Antimicrob Chemother. 2025 Aug 29:dkaf319. doi: 10.1093/jac/dkaf319. Online**

**ahead of print.**

Pharmacokinetics of rifampicin and isoniazid in patients with HIV-tuberculosis

coinfection receiving efavirenz-based antiretroviral treatment: an

ANRS12292-RIFAVIRENZ sub-study.

Gelé T(1), Atwine D(2)(3), Baudin E(4), Muyindike W(5), Mworozi K(2), Kyohairwe

R(2), Kananura K(2)(5), Logoose S(2), Nyehangane D(2), Nanjebe DKT(3), Furlan

V(6), Taburet AM(7), Bonnet M(8), Barrail-Tran A(1)(7); ANRS12292 Rifavirenz

study group.

Collaborators: Blanc FX, Harrison T, Decosterd LA, Calmy A, Jindani A, Justumus

P, Mendy Y, Michon C, Muzanye G, McIlleron H, Falissard B.

Author information:

(1)Service de Pharmacie, AP-HP. Université Paris-Saclay, Hôpital Bicêtre, 78 rue

du Général Leclerc, 94270 Le Kremlin-Bicêtre, France.

(2)Epicentre, PO Box 1956, Mbarara, Uganda.

(3)SRF Research and Training Centres, PO Box 422317, Mbarara, Uganda.

(4)Epicentre-Médecins Sans Frontières, 34, avenue Jean Jaurès, 75019 Paris,

France.

(5)Mbarara Regional Referral Hospital, Mbarara, Uganda.

(6)Service de Pharmacologie-Toxicologie, AP-HP. Université Paris-Saclay, Hôpital

Bicêtre, Le Kremlin-Bicêtre, France.

(7)Immunologie des Maladies Virales, Auto-immunes, Hématologiques et

Bactériennes, Université Paris-Saclay, Inserm, CEA, 92265 Fontenay-aux-Roses,

France.

(8)TransVIHMI, University of Montpellier, IRD/INSERM, Montpellier, France.

**BACKGROUND:** Increasing rifampicin dosing is considered a potent strategy for

shortening TB treatment duration. Although previous data among patients with

HIV-TB coinfection has shown that doubling rifampicin dosing had a small effect

on EFV concentrations, its effect on the pharmacokinetics (PK) of

antituberculosis drugs remains lacking in this population.

**OBJECTIVES:** To compare the PK of rifampicin and isoniazid with and without EFV

co-administration in patients with HIV-TB coinfection using two rifampicin

dosing regimens (10 and 20 mg/kg/day) and EFV dosing (600 and 800 mg q24h).

**METHODS:** Ninety-seven patients were assigned to three arms in a randomized

clinical trial conducted in Uganda. Plasma concentrations of rifampicin,

isoniazid, and acetyl-isoniazid were measured. PK parameters were estimated, and

statistical comparisons were made using geometric mean ratios, 90% CIs and the

pre-set 0.80-1.25 interval.

**RESULTS:** Doubling rifampicin dosing increased its Cmax and AUClast almost

3-fold. Adding EFV decreased rifampicin AUClast by 34%-40%. Isoniazid AUClast

was unaffected with EFV 600 mg q24h but decreased with EFV 800 mg q24h by 23%.

EFV increased acetyl-isoniazid concentrations, suggesting enhanced acetylation

activity. At 10 mg/kg of rifampicin, 88% of patients had Cmax below the

therapeutic range. However, at 20 mg/kg of rifampicin, 87% of patients achieved

therapeutic concentrations, ensuring effective treatment.

**CONCLUSIONS:** The study highlights the importance of adjusting rifampicin dosing

to achieve therapeutic levels in patients with coinfection. Doubling rifampicin

dosing in patients with HIV-TB coinfection increases the percentage of patients

with Cmax within the therapeutic range. Additionally, while EFV slightly affects

rifampicin and isoniazid PK, these changes are not clinically significant,

supporting the efficacy and safety of the combined regimen.

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**20. Thorax. 2025 Aug 28:thorax-2024-222170. doi: 10.1136/thorax-2024-222170. Online ahead of print.**

Challenges in respiratory medicine: the need for integrated tuberculosis and

respiratory care in low-resource settings.

Kagima JW(1)(2), Ozoh OB(3)(4), Mpagama S(5), Engel N(6), Lesosky M(7), Madan

J(8), Chakaya J(1)(2), Meghji J(9).

Author information:

(1)Department of Medicine, Kenyatta National Hospital, Nairobi, Kenya.

(2)Centre for Respiratory Diseases Research, Kenya Medical Research Institute,

Nairobi, Kenya.

(3)Department of Medicine, University of Lagos College of Medicine, Lagos,

Lagos, Nigeria.

(4)Department of Medicine, Lagos University Teaching Hospital, Surulere, Lagos,

Nigeria.

(5)Kibong'oto Infectious Diseases Hospital, Kilimanjaro, United Republic of

Tanzania.

(6)The Athena Institute, Vrije University, Amsterdam, The Netherlands.

(7)National Heart and Lung Institute, Imperial College London, London, UK.

(8)Warwick Medical School, University of Warwick, Coventry, UK.

(9)National Heart and Lung Institute, Imperial College London, London, UK

j.meghji@imperial.ac.uk.

**BACKGROUND:** Pulmonary tuberculosis (PTB) and chronic respiratory diseases (CRDs)

are intricately linked. People with PTB and CRDs experience similar symptoms,

including breathlessness, cough and chest pain. They may have similar risk

factors for disease, including smoking and occupational exposures. PTB is also a

direct cause of lung damage in the form of post-TB lung disease. However,

despite the overlap in risk factors, symptoms and sequelae, public health and

clinical care pathways for TB and CRDs remain almost entirely separate in many

low- and middle-income countries (LMICs). Those with respiratory symptoms are

directed to TB services as a first point of contact where they are known as

'people with presumptive TB', and pathways to respiratory diagnosis and care

remain largely inadequate.

**AIM:** In this opinion piece we describe opportunities for the integration of

tuberculosis (TB) and respiratory care, as a means of improving patient outcomes

in LMICs. Strategies may include upstream public health interventions to address

shared risk factors, the use of shared diagnostic pathways, the provision of

decentralised access to both TB and CRD care, and coordinated information

provision about the risk factors and symptoms of both conditions. Health-related

benefits may include more timely diagnosis of CRDs, improved CRD treatment and

care, and reduced inappropriate empirical TB treatment or retreatment. We

highlight the need for pilot models of integrated care, with robust design and

evaluation, and we note that an integrated approach may be particularly timely

given the increasing scarcity of global health donor funding.

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**21. Clin Microbiol Infect. 2025 Aug 26:S1198-743X(25)00418-5. doi:**

**10.1016/j.cmi.2025.08.020. Online ahead of print.**

Team-based, hybrid, or standard of care? Organizational models of tuberculosis

care on tuberculosis outcomes in eleven Italian hospital.

Giacomo G(1), Di Gennaro F(2), Francesco C(3), Mariantonietta P(4), Lorenzo

O(4), Federica Z(5), Giuseppe B(6), Massimo F(7), Di Gregorio S(2), Agostina

P(8), Tiziana I(7), Di Bari V(9), Marika F(4), Manco Cesari G(2), Luisa F(2),

Gianfranco P(10), Raffaella L(9), Caterina M(4), Alessia M(11), Francesca S(12),

Mariangela N(13), Salvatore R(12), De Gregorio F(13), Marinella C(2), Loredana

A(4), De Iaco G(2), Rossana L(2), Luigi R(14), Gaetano B(2), Vincenzo G(2),

Santoro CR(2), Gina G(9), Salvatore M(11), Buccoliero GB(6), Lo Caputo S(2),

Sergio C(10), Antonio C(5), Alessandro R(12), Roberto P(8), Fabrizio P(9),

Annalisa S(2), Nicola C(4).

Author information:

(1)Department of Precision and Regenerative Medicine and Jonian Area (DiMePreJ),

Clinic of Infectious Diseases, University of Bari Aldo Moro, Bari, BA, Italy.

Electronic address: g.guido13@phd.uniba.it.

(2)Department of Precision and Regenerative Medicine and Jonian Area (DiMePreJ),

Clinic of Infectious Diseases, University of Bari Aldo Moro, Bari, BA, Italy.

(3)Independent Statistician, Solagna, Italy.

(4)Department of Mental Health and Public Medicine, Section of Infectious

Diseases, University of Campania Luigi Vanvitelli, Naples, Italy.

(5)Department of Health Promotion, Mother and Child Care, Internal Medicine and

Medical Specialties "G D'Alessandro", Infectious and Tropical Disease Unit,

University of Palermo, Palermo, Italy.

(6)Infectious Disease Department, Saint Giuseppe Moscati Hospital, Taranto, TA,

Italy.

(7)UOC Malattie Infettive, ASL BA, PO Della Murgia "Fabio Perinei", Altamura,

BA, Italy.

(8)Respiratory Infectious Disease Unit, AORN dei Colli, Cotugno Hospital,

Naples, NA, Italy.

(9)Respiratory Infectious Diseases Unit, National Institute for Infectious

Diseases Lazzaro Spallanzani-IRCCS, Rome, RM, Italy.

(10)UOC Malattie Infettive, Ospedale Vittorio Emanuele II, ASL BT, Bisceglie,

BT, Italy.

(11)UOC Malattie Infettive, Ospedale Antonio Perrino, Brindisi, BR, Italy.

(12)Department of Medical and Surgical Sciences, Infectious and Tropical Disease

Unit, 'Magna Graecia' University of Catanzaro, Catanzaro, Italy.

(13)Department of Medical and Surgical Sciences, Infectious Diseases Unit,

University of Foggia, Foggia, FG, Italy.

(14)Microbiology and Virology Unit, University of Bari, University Hospital

Policlinico, Bari, Italy.

**OBJECTIVES:** Tuberculosis (TB) continues to pose challenges in high-income

countries, among migrant and socioeconomically vulnerable populations. Treatment

discontinuity and loss to follow-up (LTFU) remain critical barriers to TB

control. This study evaluated the impact of three organizational models of TB

care on clinical and programmatic outcomes in Italy.

**METHODS:** We conducted a multicenter study including all TB patients diagnosed

between 2021 and 2024 in 11 hospitals in five regions. Centers were categorized

into three care models: (i) TB-Team (structured care with trained staff,

dedicated outpatient clinics, and proactive follow-up); (ii) Hybrid center (HC);

and (iii) Standard of Care (SOC). Primary outcomes included hospital length of

stay, incidence and severity of adverse events, treatment completion, and LTFU.

Mixed-effect regression models adjusted for confounders.

**RESULTS:** Of 717 pan-susceptible and mono-resistant TB patients, 375 (52.3%) were

treated in TB-team centers, 175 (24.4%) in HC, and 167 (23.3%) in SOC centers.

Treatment completion was higher in TB-team (327/375, 87.2%) vs. HC (116/162,

71.6%) and SOC centers (89/158, 56.3%) (p<0.0001), while LTFU was lowest in

TB-team (35/375, 9.3%) vs. HC (44/162 27.2%) and SOC (63/158, 39.9%) (p<0.0001).

Hospital stay was shorter in TB-team (median 26 days, IQR 15-55) and HC

(35 days, IQR 22-62) compared to SOC (50 days, IQR 22-82) (p<0.0001). The

occurrence of adverse events was similar (p=0.54), with lower severity in

TB-team and HC. Adjusted analyses confirmed lower risk of incomplete treatment

(OR 0.10, 95% CI 0.03 to 0.30), LTFU (OR 0.09, 95% CI 0.04 to 0.23) and severe

adverse events (OR 0.40, 95% CI 0.17 to 0.95) in TB Team vs. SOC.

**CONCLUSIONS:** The TB-dedicated care model was associated with improved outcomes,

fewer severe adverse events, higher treatment completion rates, and lower LTFU.

While hybrid models conferred intermediate benefit, implementation of TB care

ensured consistent gains. These findings support scaling up TB team-based models

to strengthen TB control and align with elimination targets.

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DOI: 10.1016/j.cmi.2025.08.020

PMID: 40876575

**22. JCI Insight. 2025 Aug 28:e195947. doi: 10.1172/jci.insight.195947. Online ahead of print.**

Development and Preclinical Evaluation of Next-generation ΔsigH-based Live

Candidate Vaccines.

Arora G(1), Munson CW(1), Ahmed M(2), Shivanna V(1), Devi A(1), Devireddy VS(1),

Antony B(1), Hall-Ursone S(1), Gonzalez OD(1), Dick E Jr(1), Jagannath C(3),

Alvarez X(1), Mehra S(1), Khader SA(2), Singh DK(1), Kaushal D(1).

Author information:

(1)Texas Biomedical Research Institute, San Antonio, United States of America.

(2)Department of Microbiology, University of Chicago, Chicago, United States of

America.

(3)Houston Methodist Research Institute, Houston, United States of America.

To radically diminish TB incidence and mortality by 2035, as set out by the WHO

End TB Strategy, there is a desperate need for improved TB therapies and a more

effective vaccine against the deadly pathogen Mycobacterium tuberculosis (Mtb).

Aerosol vaccination with the MtbΔsigH mutant protects two different species of

NHPs against lethal TB challenge by invoking vastly superior T and B cell

responses in the lungs through superior antigen-presentation and

interferon-conditioning. Since the Geneva consensus on essential steps towards

the development of live mycobacterial vaccines recommends that live TB vaccines

must incorporate at least two independent gene knock outs, we have now generated

several rationally designed, double (DKO)- and triple (TKO) knock-out mutants in

Mtb, each containing the ΔsigH deletion. Here, we report preclinical studies in

the rhesus macaque model of aerosol infection and SIV/HIV co-infection, aimed at

assessing the safety of these MtbΔsigH - based DKOs and TKOs. We found that most

of these mutant strains are attenuated in both immunocompetent and

SIV-co-infected macaques and combinatorial infection with these generated strong

cellular immune responses in the lung, akin to MtbΔsigH. Aerosol infection with

these KO strains elicited inducible Bronchus Associated Lymphoid Tissue (iBALT),

which is a correlate of protection from TB.

DOI: 10.1172/jci.insight.195947

PMID: 40875531

**23. Arch Microbiol. 2025 Aug 28;207(10):239. doi: 10.1007/s00203-025-04429-6.**

DNA gyrase-inhibitory antimicrobial anthraquinone from the endophytic

Sordariomycetes fungus Diaporthe perseae.

Manzano JAH(1)(2), Abanto JCD(3), Dayo BAF(3), Llames LCJ(4), Gonzaga MGE(5),

Brogi S(6)(7), Macabeo APG(8).

Author information:

(1)Department of Biological Sciences, College of Science, and UST Laboratories

for Vaccine Science, Molecular Biology, and Biotechnology, University of Santo

Tomas, España Blvd., Manila, 1015, Philippines. jhmanzano@ust.edu.ph.

(2)Research Center for the Natural and Applied Sciences, University of Santo

Tomas, España Blvd., Manila, 1015, Philippines. jhmanzano@ust.edu.ph.

(3)Department of Chemistry, College of Science, University of Santo Tomas,

España Blvd., Manila, 1015, Philippines.

(4)Research Center for the Natural and Applied Sciences, University of Santo

Tomas, España Blvd., Manila, 1015, Philippines.

(5)College of Arts and Sciences, President Ramon Magsaysay State University,

Iba, 2201, Zambales, Philippines.

(6)Department of Pharmacy, University of Pisa, Via Bonanno 6, Pisa, 56126,

Italy.

(7)Bioinformatics Research Center, School of Pharmacy and Pharmaceutical

Sciences, Isfahan University of Medical Sciences, Isfahan, 81746-73461, Iran.

(8)Department of Microbial Drugs, Helmholtz Center for Infection Research,

Braunschweig, Inhoffenstrasse 7, 38124, Braunschweig, Germany.

allanpatrick.macabeo78@gmail.com.

Fungi of the order Diaporthales are prolific sources of antimicrobial secondary

metabolites. In this paper, we describe antimicrobial and antituberculosis

anthraquinones (AQs) from Diaporthe perseae, an endophytic fungus isolated and

identified from the endemic Philippine medicinal plant Uvaria alba (Annonaceae).

Large-scale rice fermentation of D. perseae yielded an ethyl acetate extract

which was subjected to a series of chromatographic purification to yield three

compounds. Spectroscopic analyses allowed the identification of the

anthraquinone compounds citreorosein (1), skyrin (2), and rugulosin A (3). AQs 1

and 3 showed broad-spectrum against Gram-positive bacteria (Micrococcus luteus,

Bacillus subtilis, and Staphylococcus aureus) (MIC = 1.0-2.0 µg/mL), however

only 3 demonstrated strong inhibition against Gram-negative bacterial strains

(Escherichia coli, Pseudomonas aeruginosa, and Chromobacterium violaceum) and

non-TB mycobacteria (Mycobacterium smegmatis) (MIC = 8.25-66.0 µg/mL). AQ 3 also

exhibited inhibition against both M. tuberculosis (Mtb) H37Rv (Microplate Alamar

Blue Assay; MABA MIC = 29.2 µg/mL) and its non-replicating persistent strain

(Low-Oxygen Recovery Assay; LORA MIC = 30.3 µg/mL). To explore the potential

mechanism of 3, DNA supercoiling assay was performed. Thus, rugulosin A (3)

displayed inhibition of Mtb. DNA gyrase, an enzyme necessary for genomic

replication via ATP-dependent DNA relaxation mechanisms. Molecular docking and

molecular dynamics revealed strong, stable binding affinity of 3 (BE =

-9.5 kcal/mol) and its tautomer 4 (BE = -9.6 kcal/mol) within the active pocket

of the MtbDNA gyrase. Overall, rugulosin A (3) represents a promising antibiotic

prototype with in vitro and in silico activity against M. tuberculosis, and

identifies DNA gyrase as therapeutic target for anthraquinone

antimycobacterials.

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**24. mBio. 2025 Aug 28:e0158525. doi: 10.1128/mbio.01585-25. Online ahead of print.**

Inflammation and B cell activation define a plasma proteome signature predicting

tuberculosis in people with HIV.

Kusejko K(1)(2), Arefian M(3), Duroux D(4)(5)(6), Zeeb M(1)(2), Dollé C(1),

Hoffmann M(7), Labhardt N(8)(9), Wandeler G(10), Cavassini M(11), Haller S(12),

Bernasconi E(13)(14), Russenberger D(1), Kouyos RD(1)(2), Günthard HF(1)(2),

Collins BC(3), Nemeth J(1); Swiss HIV Cohort Study.

Author information:

(1)Department of Infectious Diseases and Hospital Epidemiology, University

Hospital Zurich and University of Zurich, Zürich, Switzerland.

(2)Institute of Medical Virology, University of Zurich, Zürich, Switzerland.

(3)School of Biological Sciences, Queen's University Belfast, Belfast, United

Kingdom.

(4)ETH Zurich, AI Center, Zürich, Switzerland.

(5)Department of Biosystems Science and Engineering, ETH Zurich, Basel,

Switzerland.

(6)Department of Quantitative Biomedicine, University of Zurich, Zürich,

Switzerland.

(7)Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital

Olten, Olten, Switzerland.

(8)Division of Clinical Epidemiology, Department of Clinical Research,

University Hospital Basel, Basel, Switzerland.

(9)University of Basel, Basel, Switzerland.

(10)Division of Infectious Diseases, Bern University Hospital, University of

Bern, Bern, Switzerland.

(11)Division of Infectious Diseases, University Hospital of Lausanne, Lausanne,

Switzerland.

(12)Division of Infectious Diseases, Infection Prevention and Travel Medicine,

HOCH Health Ostschweiz, St. Gallen, Switzerland.

(13)Division of Infectious Diseases, Ente Ospedaliero Cantonale, Lugano,

Switzerland.

(14)University of Geneva and University of Southern Switzerland, Lugano,

Switzerland.

Improved biomarkers for predicting progression to active tuberculosis (TB) are

urgently needed, especially in people with HIV, who are at elevated risk. We

used high-throughput plasma proteomics and machine learning to identify

signatures associated with TB progression in this population. From the Swiss HIV

Cohort Study, we analyzed plasma samples collected at least 6 months before TB

diagnosis from 91 participants who later developed TB. We selected 293 controls

matched for demographic and clinical parameters who remained TB-free to achieve

a risk score specific to active TB. In total, 583 samples were analyzed, with

613-1,283 proteins quantified per sample. A random forest classifier predicted a

significantly higher median probability of TB progression for cases (33%) than

for controls (16%; P < 0.001). In this matched population, the score achieved an

area under the receiver-operating characteristic curve of 0.77, an area under

the precision-recall curve (AUPRC) of 0.60 (as compared to an expected AUPRC of

0.29), as well as a specificity of 87.3% and a sensitivity of 58.6% using the

optimal threshold of 0.311. The plasma proteome of individuals who progressed to

active TB showed a distinct shift toward systemic inflammation, B cell

activation, and immunoglobulin production. Independent of progression to active

TB, the proteome score correlated with broader indicators of immune suppression,

including lower CD4 counts and unsuppressed HIV RNA. This suggests that

integrating proteomic and clinical data could enhance the overall predictive

power of the score.IMPORTANCEWe still lack reliable tools to predict who will

develop tuberculosis (TB) among people with HIV. Moreover, the underlying

biological events driving progression remain poorly understood. Our study

reveals early immune changes that include unexpected alterations in B cell

activation and antibody responses. These findings suggest that humoral immunity

may play a more important role in TB pathogenesis than previously recognized and

offer promising new directions for biomarker discovery and targeted prevention.

DOI: 10.1128/mbio.01585-25

PMID: 40874618

**25. Lancet Digit Health. 2025 Aug 26:100884. doi: 10.1016/j.landig.2025.100884.**

**Online ahead of print.**

Computer-aided reading of chest radiographs for paediatric tuberculosis: current

status and future directions.

DuPont M(1), Castro R(2), Kik SV(3), Palmer M(4), Seddon JA(5), Jaganath D(6).

Author information:

(1)Division of Pediatric Emergency Medicine, Baylor College of Medicine,

Houston, TX, USA.

(2)Division of Pulmonary and Critical Care Medicine, University of California

San Francisco, San Francisco, CA, USA; Center for Tuberculosis, Institute for

Global Health Sciences, University of California San Francisco, San Francisco,

CA, USA.

(3)The Hague, Netherlands; FIND, Geneva, Switzerland.

(4)Desmond Tutu TB Centre, Department of Paediatrics and Child Health,

Stellenbosch University, Cape Town, South Africa.

(5)Desmond Tutu TB Centre, Department of Paediatrics and Child Health,

Stellenbosch University, Cape Town, South Africa; Department of Infectious

Disease, Imperial College London, London, UK.

(6)Division of Pulmonary and Critical Care Medicine, University of California

San Francisco, San Francisco, CA, USA; Center for Tuberculosis, Institute for

Global Health Sciences, University of California San Francisco, San Francisco,

CA, USA; Division of Pediatric Infectious Diseases, University of California San

Francisco, San Francisco, CA, USA. Electronic address: devan.jaganath@ucsf.edu.

Computer-aided detection (CAD) systems for automated reading of chest x-rays

(CXRs) have been developed and approved for tuberculosis triage in adults but

not in children. However, CXR is frequently the only adjunctive tool for

clinical assessment in the evaluation of paediatric tuberculosis in primary care

settings, and children would benefit from CAD models that can detect their

unique clinical and radiographic features. To advance CAD for childhood

tuberculosis, large, diverse paediatric CXR datasets linked to standardised

tuberculosis classifications are required. These datasets would be used to train

and validate paediatric-specific models for tuberculosis screening, diagnosis,

and severity stratification. Previous studies on CAD algorithms for reading

paediatric CXRs have highlighted promising approaches, including the use of

transfer learning with existing deep learning models. Including data from

children in CAD models is essential to improve equity and reduce the global

burden of tuberculosis disease.

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**26. Intern Med. 2025 Aug 28. doi: 10.2169/internalmedicine.5794-25. Online ahead of print.**

The Prognostic Value of The Neutrophil-to-lymphocyte Ratio in Older Patients

with Pulmonary Tuberculosis.

Okada Y(1), Kumamoto M(1), Tomita D(1), Koyama Y(1), Yoshino E(1), Tanaka S(1),

Bandoh C(1), Tamaki S(1)(2), Muro S(2).

Author information:

(1)Department of Internal Medicine, National Hospital Organization Nara Medical

Center, Japan.

(2)Department of Respiratory Medicine, Nara Medical University, Japan.

**Objective** The neutrophil-to-lymphocyte ratio (NLR) is a readily available

biomarker associated with the prognosis of several diseases. However, the

available studies investigating the association between NLR and prognosis in

older patients with pulmonary tuberculosis (PTB) are insufficient. We aimed to

clarify the association between the peripheral NLR and the prognosis in older

patients with PTB. **Methods** We retrospectively examined 115 PTB patients aged ≥65 years. Pretreatment blood tests and chest computed tomography were performed to assess mortality at 30 and 365 days after treatment initiation (Day30 and

Day365). **Results** NLR was an associated factor of mortality at Day30 after

adjusting for the serum hemoglobin and albumin levels (odds ratio [OR], 1.13;

95% confidence interval [CI], 1.03-1.24). However, no significant association

was found between NLR and mortality at Day365 (OR, 1.04; 95% CI, 0.956-1.13). To

evaluate the usefulness of NLR in predicting mortality on Day30, we analyzed the

receiver operating characteristic (ROC) curve. The area under the curve of the

NLR was 0.831 (95% CI, 0.733-0.929). Using an ROC curve analysis, we determined

that the effective cut-off value of the NLR for predicting prognosis was 5.664

(sensitivity, 67.0%; specificity, 88.9%). We divided the patients into two

groups based on the previously mentioned cut-off values. The survival rate at 30

days was significantly lower in the group with an NLR≥5.664 than in the group

with an NLR<5.664. **Conclusion** The NLR may be a useful predictive factor for the

short-term prognosis in older patients with PTB.

DOI: 10.2169/internalmedicine.5794-25

PMID: 40866256

**27. PLoS One. 2025 Aug 26;20(8):e0330208. doi: 10.1371/journal.pone.0330208.**

**eCollection 2025.**

Effectiveness of tuberculosis preventive treatment on disease incidence among

people living with HIV/AIDS: A systematic review and meta-analysis.

Silva Júnior JNB(1)(2), Leal GDC(1), Ferreira QR(1), Andrade LKA(1), Ballestero

JGA(1), Santos VS(3), Pescarini JMA(4), Trajman A(5)(6), Arakaki-Sanchez D(7),

Bartholomay P(8), de Paula Andrade RL(1), Pelissari D(7), Palha PF(1).

Author information:

(1)Ribeirão Preto College of Nursing, University of São Paulo, Ribeirão Preto,

SP, Brazil.

(2)Institute of Scientific and Technological Communication and Information in

Health, Oswaldo Cruz Foundation, Rio de Janeiro, RJ, Brazil.

(3)Department of Medicine, Federal University of Sergipe, Lagarto, SE, Brazil.

(4)London School of Hygiene & Tropical Medicine, London, GLA, United Kingdom.

(5)Research Institute, McGill University Health Center, Montréal, QC, Canada.

(6)Faculty of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro,

Brazil.

(7)Ministry of Health, National Tuberculosis Programme, Brasilia, DF, Brazil.

(8)Ministry of Health, National Center for Epidemiological Intelligence and

Genomic Surveillance, Brasilia, DF, Brazil.

**BACKGROUND:** Clinical trials have shown the protective efficacy of tuberculosis

preventive treatment (TPT) for averting disease and death from tuberculosis

among people living with HIV/AIDS (PLHIV). TPT has been recommended for PLHIV

since the 1980s. However, tuberculosis is still the first cause of death in

PLHIV.

**OBJECTIVE:** We aimed to summarize the evidence related to the real-world

effectiveness of TPT on tuberculosis incidence among PLHIV.

**METHOD:** This is a systematic review and meta-analysis of observational cohort

studies. The search was carried out in PubMed (via MEDLINE), Embase, LILACS,

Scopus and Web of Science databases. Free and controlled vocabulary was used for

the searches, with no restrictions on language or publication period. Studies

reporting hazard ratios (HR) for tuberculosis incidence among PLHIV who received

TPT were pooled using random-effects meta-analysis models. Meta-regression was

performed to assess whether study-level characteristics accounted for

heterogeneity, as evaluated by Cochran's I² statistic. Study quality was

appraised using the Newcastle-Ottawa Scale. This study was registered with

PROSPERO (CRD42024586273).

**RESULTS:** Among 8,330 screened studies, 34 were included, with nine contributing

to the meta-analysis. TPT was associated with a 63% reduction in tuberculosis

incidence risk (HR = 0.37, 95% CI: 0.28-0.48; I² = 43%). Children exhibited

consistent stronger protection (82% risk reduction, HR = 0.18, 0.09-0.37;

I² = 0%) than adults (56% reduction, HR = 0.44, 0.37-0.53; I² = 21%).

**CONCLUSION:** In real world conditions, TPT significantly and substantially

reduces tuberculosis incidence in PLHIV, with consistent evidence of stronger

protective effects in children. Despite some heterogeneity among adult studies,

the pooled evidence confirms the protective effectiveness previously observed in

clinical trials. These findings reinforce the global recommendation for broad

implementation of TPT among PLHIV.

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original author and source are credited.

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PMID: 40857234 [Indexed for MEDLINE]

**28. Glob Health Res Policy. 2025 Aug 25;10(1):37. doi: 10.1186/s41256-025-00437-7.**

Impact of COVID-19 pandemic, and the mediating role of hospital caseload and

severity on mortality of hospitalised tuberculosis patients in Thailand.

Zayar NN(1), Chotipanvithayakul R(1), Geater AF(1), Htet KKK(1), Ngamphiw C(2),

Chongsuvivatwong V(3).

Author information:

(1)Department of Epidemiology, Faculty of Medicine, Prince of Songkla

University, 15 Kanjanavanich Road, Hat Yai, Songkhla, 90110, Thailand.

(2)National Biobank of Thailand, National Science and Technology Development

Agency, Khlong Luang, Pathum Thani, 12120, Thailand.

(3)Department of Epidemiology, Faculty of Medicine, Prince of Songkla

University, 15 Kanjanavanich Road, Hat Yai, Songkhla, 90110, Thailand.

cvirasak@medicine.psu.ac.th.

**BACKGROUND:** The COVID-19 hospital caseload indicates the quality of hospital

care, as resources were redirected to address the surge in COVID-19 cases. The

study aimed to evaluate the impact of COVID-19 hospital caseload on hospital

tuberculosis (TB) case fatality rate (CFR) mediated by the TB caseload and

severity of patients.

**METHODS:** A retrospective analysis of TB patients' hospital admission data in

Thailand extracted from the Thai Health Information Portal database between

January 2017 and September 2022. Charlson Comorbidity Index (CCI) was used to

determine the severity of hospitalised TB patients. An interrupted time series

analysis, lag time analysis and serial mediation analysis were done.

**RESULTS:** During COVID-19 pandemic, there was a 12.9% decrease in monthly

hospital TB caseload, and a 14.1% increase in monthly TB hospital CFR compared

to the counterfactual scenario had there been no COVID-19. COVID-19 hospital

caseload had a strong negative correlation with TB hospital caseload (r =

- 0.60, p-value = < 0.001), but a strong positive correlation with TB hospital

CFR (r = 0.74, p-value = < 0.001) during the same month. An increase in average

CCI score of 0.1 was associated with an increase of 2.3 deaths per 100 TB

admissions. After adjusting the TB caseload and CCI of TB patients admitted to

the hospital, no association was found between COVID-19 hospital caseload and

the hospital CFR of TB patients.

**CONCLUSIONS:** The increase in TB hospital CFR during COVID-19 pandemic was likely

driven by a higher proportion of severe cases being admitted, rather than a

decline in hospitals' quality of care.

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**29. Rev Gaucha Enferm. 2025 Aug 25;46(spe1):e20240309. doi:**

**10.1590/1983-1447.2025.20240309.en. eCollection 2025.**

Characterization of tuberculosis cases in the indigenous population of Mato

Grosso, 2011-2020.

[Article in English, Portuguese]

Silva WA(1), Kuss GCN(1), Lacerda AB(2), Couto RM(3), Arruda VL(4), Silva

PRS(1), Espinosa OA(5), Lima JC(1).

Author information:

(1)Universidade Federal de Mato Grosso. Faculdade de Enfermagem. Cuiabá. Mato

Grosso. Brasil.

(2)Universidade de São Paulo. Faculdade de Saúde Pública. São Paulo, São Paulo,

Brasil.

(3)Universidade Federal de São Paulo. Departamento de Medicina Preventiva. São

Paulo, São Paulo, Brasil.

(4)Universidade Federal de São Paulo. Escola Paulista de Enfermagem. São Paulo,

São Paulo, Brasil.

(5)Faculdade do Pantanal. Cáceres, Mato Grosso, Brasil.

**OBJECTIVE:** To analyze the epidemiological and clinical profile of tuberculosis

in the indigenous population of Mato Grosso (2011-2020).

**METHOD:** This is a descriptive study using data recorded in the Information

System for Notifiable Diseases (Sistema de Informação de Agravos de Notificação,

SINAN). Statistical analyses were performed, stratified by sociodemographic and

clinical variables, comparing tuberculosis cases in the general and indigenous

populations of Mato Grosso (Brazil), using the chi-square and Fisher's exact

tests in SPSS® 25.0. The incidence rates were calculated per 100,000 inhabitants

and analyzed over the years and by geographic area via GeoDa® 1.20.0.36 and

Qgis® 3.32.1. The data were aggregated by regional health departments.

**RESULTS:** A total of 11,288 tuberculosis cases were recorded in the general

population and 879 cases in indigenous people, with mean incidence values of

36.3 and 173.1 cases per 100,000 inhabitants, respectively. Indigenous

individuals had a higher proportion of women (48.8% vs. 30.3%, p<0.001), young

people (10-17 years old: 21.4% vs. 2.3%, p<0.001), pulmonary forms (97.4% vs.

90.0%, p<0.001) and a higher cure rate (88.9% vs. 76.5%, p<0.001). The spatial

distribution was heterogeneous in the indigenous population, with predominance

in remote areas of the state.

**CONCLUSION:** Tuberculosis had higher incidence in the indigenous population of

Mato Grosso (2011-2020) when compared to the general population. Among

indigenous individuals, there was a higher proportion of affected women and

young people, predominance of pulmonary forms and lower frequency of

comorbidities.

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PMID: 40862462

**30. Am J Trop Med Hyg. 2025 Aug 26:tpmd250313. doi: 10.4269/ajtmh.25-0313. Online**

**ahead of print.**

Scapular Tuberculosis.

Nakamoto K(1), Fukushima S(1), Oguni K(1), Hagiya H(1).

Author information:

(1)Department of Infectious Diseases, Okayama University Hospital, Okayama,

Japan.

DOI: 10.4269/ajtmh.25-0313

PMID: 40858144

**31. Sci Rep. 2025 Aug 25;15(1):31309. doi: 10.1038/s41598-025-15855-3.**

Antitubercular drug induced liver injury among tuberculosis patients in central

Ethiopia.

Petros Z(1)(2), Tamirat A(3), Assefa W(4).

Author information:

(1)Department of Pharmacy, College of Medicine and Health Sciences, Wachemo

University, Hosaina, Ethiopia. zelalemp@yahoo.com.

(2)Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College

of Medicine and Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia.

zelalemp@yahoo.com.

(3)Department of Pharmacy, College of Medicine and Health Sciences, Wachemo

University, Hosaina, Ethiopia.

(4)Quality assurance and enhancement directorate, College of Medicine and Health

Sciences, Wachemo University, Hosaina, Ethiopia.

Tuberculosis (TB) is a curable disease that can be treated with antitubercular

(anti-TB) drugs that have markedly reduced mortality due to the disease.

However, the drugs may cause liver injury, which is associated with increased

morbidity due to acute liver failure, disease progression, and drug resistance.

There is a scarcity of evidence on the prevalence and predictors of anti-TB

drug-induced liver injury (ATDILI). The aim of this study is to the assess

prevalence, predictors, and clinical features of ATDILI in the health centers of

Hossana town, Central Ethiopia. In a prospective cohort study, newly diagnosed

TB patients (N = 219) receiving first-line anti-TB drugs were enrolled in three

selected health centers in Hossana town, Central Ethiopia. Liver function tests

were assessed before and four and eight weeks after drug treatment initiation.

Patients that had abnormal liver biochemistry prior to treatment and patients

positive for either hepatitis B or C viral antibody were excluded. Thirty-five

study participants (16.0%) developed ATDILI. Two of them (5.7%) had severe

ATDILI. Nausea, vomiting, and anorexia were the most frequently observed

symptoms. In multivariable analysis, ATDILI was significantly associated with

gender (adjusted odds ratio, AOR = 2.57, 95% CI = 1.11-5.91, P = 0.027), age

(AOR = 1.05, 95% CI = 1.01-1.10, P = 0.019), body mass index (AOR = 0.81, 95%

CI = 0.69-0.95, P = 0.009), and HIV status (AOR = 6.73, 95% CI = 1.81-25.09,

P = 0.005). The results of the study suggest that the prevalence of ATDILI is

high among TB patients getting treatment in the health centers in Hossana town,

Central Ethiopia. Thus, patients who are female, older, have a low body mass

index, and are HIV positive should have their liver function regularly monitored

to reduce ATDILI.

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PMID: 40854941 [Indexed for MEDLINE]

**32. Comput Biol Med. 2025 Aug 25;197(Pt A):110991. doi:**

**10.1016/j.compbiomed.2025.110991. Online ahead of print.**

Computational analysis of Phanera sirindhorniae flavonoids as potential

inhibitors of Mycobacterium tuberculosis DNA gyrase ATPase.

Kamsri P(1).

Author information:

(1)Division of Chemistry, Faculty of Science, Nakhon Phanom University, Nakhon

Phanom, 48000, Thailand. Electronic address: pharit.kamsri@npu.ac.th.

The rise of drug-resistant Mycobacterium tuberculosis underscores the urgent

need for safe and bioavailable compounds that target essential bacterial

pathways. ATPase domain of DNA gyrase subunit B (GyrB) is a mechanistically

distinct and druggable site involved in DNA supercoiling and energy metabolism.

In this study, we employed a structure- and system-guided computational pipeline

to identify natural flavonoids with multi-target inhibitory potential against

GyrB. Naringenin, taxifolin, and quercetin were selected from an initial

flavonoid library based on their predicted ATPase inhibition, anti-tuberculosis

(TB) activity, and pharmacokinetic properties. Molecular docking and extended

molecular dynamics (MD) simulations (3 × 500 ns) validated stable binding poses,

with molecular mechanics generalized born surface area (MM-GBSA) calculations

ranking taxifolin as the most energetically favorable (-25.6 kcal/mol),

supported by persistent interactions with Asp79, and minimal conformational

drift. Multi-omics analysis revealed the downregulation of GyrB, ParE, and AtpD,

whereas metabolomic shifts in NAD+/NADH and TCA intermediates confirmed redox

and respiratory disruptions. Physiologically based pharmacokinetic simulations

showed that naringenin achieved the highest predicted lung exposure (0.546 μM at 300 mg), whereas taxifolin offered the best overall balance between binding affinity, exposure, and safety. Synergy modeling with rifampicin identified taxifolin as the top candidate (ZIP synergy score: +4.3). These findings highlight taxifolin and naringenin as promising ATPase-targeting adjuncts for TB therapy and demonstrate how integrated MD and system pharmacology can guide the rational repurposing of natural products.

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PMID: 40857815

**33. Am J Forensic Med Pathol. 2025 Aug 27. doi: 10.1097/PAF.0000000000001071. Online ahead of print.**

Disseminated Tuberculosis: When Antemortem Testing Fails and Autopsy Prevails.

Auen T(1), Mitzel H(1), Linde E(2), Yuil-Valdes A(1).

Author information:

(1)Department of Pathology and Microbiology, Nebraska Medical Center, University

of Nebraska Medical Center, Omaha, NE.

(2)Physicians Laboratory Services Omaha, NE.

DOI: 10.1097/PAF.0000000000001071

PMID: 40856776

**34. Infect Dis (Lond). 2025 Aug 26:1-9. doi: 10.1080/23744235.2025.2546488. Online ahead of print.**

Evaluating factors influencing tuberculosis treatment outcomes and the impact of

COVID-19 on TB incidence in Bengaluru, India (2017-2023).

Srinivasan S(1), D H(1), R H SR(1), V D(1).

Author information:

(1)Department of Pharmacy, Aditya Bangalore Institute of Pharmacy Education and

Research, Bengaluru, India.

**BACKGROUND:** Tuberculosis (TB) remains a major public health issue in Bengaluru,

India. This study analyzes TB trends, treatment outcomes, and the impact of

COVID-19 on TB incidence from 2017 to 2023.

**METHODS:** Logistic regression analysis was used to identify factors influencing

TB treatment outcomes. An Interrupted Time Series (ITS) analysis using an ARIMA

(AutoRegressive Integrated Moving Average) model was used to assess the impact

of COVID-19 on TB incidence.

**RESULTS:** Among 71,883 TB cases, age ≥65 years had increased the risk of

unsuccessful outcomes for pulmonary TB (PTB) (adjusted odds ratio [aOR] 2.54;

95% confidence interval [CI], 2.24-2.89) and extrapulmonary TB (EPTB) (aOR 3.72;

CI, 3.06-4.52). Females had lower odds than males in PTB (aOR 0.72; CI,

0.67-0.78) and EPTB (aOR 0.77; CI, 0.68-0.86). Diabetics had lowered risk for

PTB (aOR 0.62; CI, 0.57-0.68) but increased risk for EPTB (aOR 1.44; CI,

1.24-1.67). HIV cases had increased risk in PTB (aOR 1.96; CI, 1.67-2.31) and

EPTB (aOR 2.88; CI, 2.32-3.57). Interaction analysis in PTB showed diabetics

with ages 35-44 and 45-54 was associated with lower risk (aOR 0.66; CI,

0.44-0.99; aOR 0.67; CI, 0.46-0.99). ITS analysis showed a 24.3% average decline

in TB notifications in 2020, reaching a maximum decline of 40.5% in April.

**CONCLUSION:** This study highlights factors affecting TB treatment outcomes and

the significant impact of COVID-19 on TB trends in Bengaluru, providing insights

to improve TB control and mitigate future pandemic impacts.

DOI: 10.1080/23744235.2025.2546488

PMID: 40855923

**35. Zoonoses Public Health. 2025 Aug 25. doi: 10.1111/zph.70008. Online ahead of**

**print.**

Mycobacterium bovis Infection in Cats: Zoonotic Transmission.

Barandiaran S(1)(2), Marfil MJ(2), Yaafar N(3), Ferrer MF(4)(5), Fajardo S(6),

Salvador MF(7), Biscia M(8), Zumárraga MJ(9), Sarradell JE(8).

Author information:

(1)CONICET-Universidad de Buenos Aires, Instituto de Investigaciones en

Producción Animal (INPA), Buenos Aires, Argentina.

(2)Universidad de Buenos Aires, Facultad de Ciencias Veterinarias, Cátedra de

Enfermedades Infecciosas, Buenos Aires, Argentina.

(3)Cátedra de Farmacología y Terapéutica, Facultad Ciencias Veterinarias,

Universidad Nacional de Rosario, Rosario, Santa Fe, Argentina.

(4)Programa de Epidemiología de la Provincia de Santa Fe, Santa Fe, Argentina.

(5)Hospital Privado de Rosario, Rosario, Santa Fe, Argentina.

(6)Centro Regional de Estudios bioquímicos de la Tuberculosis, Municipalidad de

Rosario, Rosario, Santa Fe, Argentina.

(7)Laboratorio Veterinario Salvador, Rosario, Santa Fe, Argentina.

(8)Cátedra de Patología General y Especial, Facultad de cs. Veterinarias,

Universidad Nacional de Rosario, Rosario, Santa Fe, Argentina.

(9)Centro de Investigación en cs. Veterinarias y Agronómicas (CICVyA), CNIA,

Instituto de Agrobiotecnología y Biología Molecular (IABIMO) UEDD CONICET-INTA,

Buenos Aires, Argentina.

**INTRODUCTION:** Tuberculosis caused by Mycobacterium bovis is an infectious

disease of worldwide relevance, with a growing concern for its zoonotic

potential. Although cattle are the primary host, infections in companion animals

have been reported, raising new public health concerns.

**METHODS:** Four cases of M. bovis infection in two cohabiting cats and two humans,

one being the pet owner and the other a veterinarian, are analysed.

Microbiological and molecular diagnostic techniques were employed, including

culture, PCR, and genotyping through spoligotyping.

**RESULTS:** The presence of M. bovis was confirmed in both felines, identifying the

same spoligotype (SB0140). Subsequently, the infection was documented in the pet

owner, who had no history of contact with livestock, and in a veterinarian who

sustained a needlestick injury during sample collection.

**CONCLUSIONS:** These findings highlight the risk of zoonotic tuberculosis

originating from companion animals, even in the absence of direct exposure to

livestock. The results underscore the need to strengthen diagnostic and

surveillance strategies in non-traditional species and emphasise the importance

of adopting a comprehensive One Health approach to prevent and mitigate

transmission between animals and humans, particularly in regions where bovine

tuberculosis is endemic.

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PMID: 40855579

**36. Nat Ecol Evol. 2025 Aug 25. doi: 10.1038/s41559-025-02837-x. Online ahead of**

**print.**

Twenty years of tuberculosis-driven selection shaped the evolution of the

meerkat major histocompatibility complex.

Müller-Klein N(1), Risely A(2)(3), Wilhelm K(2), Riegel V(2), Manser M(4)(5)(6),

Clutton-Brock T(5)(6)(7), Silver L(8)(9), Santos PSC(2), Melville DW(#)(2),

Sommer S(#)(2).

Author information:

(1)Institute for Evolutionary Ecology and Conservation Genomics, Ulm, Germany.

Nadine.Mueller-Klein@uni-ulm.de.

(2)Institute for Evolutionary Ecology and Conservation Genomics, Ulm, Germany.

(3)School of Science, Engineering, and the Environment, Salford University,

Salford, UK.

(4)Department of Evolutionary Biology and Environmental Studies, University of

Zurich, Zurich, Switzerland.

(5)Mammal Research Institute, University of Pretoria, Pretoria, South Africa.

(6)Kalahari Research Centre, Kuruman River Reserve, Northern Cape, South Africa.

(7)Large Animal Research Group, Department of Zoology, University of Cambridge,

Cambridge, UK.

(8)School of Life and Environmental Sciences, University of Sydney, Camperdown,

New South Wales, Australia.

(9)Australian Research Council Centre of Excellence for Innovations in Peptide

and Protein Science, University of Sydney, Camperdown, New South Wales,

Australia.

(#)Contributed equally

Pathogen-mediated balancing selection (PMBS) drives host evolution across the

tree of life. Distinguishing between the three main mechanisms underlying PMBS,

that is, rare-allele advantage, fluctuating selection and heterozygote

advantage, remains difficult, limiting our understanding of frequency-dependent

adaptations by hosts and counter-adaptation by pathogens. Here we leverage

immune genetic and disease surveillance data from over 1,500 wild meerkats

(Suricata suricatta) to track how selection by the tuberculosis (TB)-causing

Mycobacterium suricattae shaped the evolution of the meerkats' major

histocompatibility complex (MHC) over two decades. Compared with neutral genetic

markers, we detect more rapid differentiation and recycling of alleles at the

MHC-DRB loci, suggesting that TB imposes strong PMBS on wild meerkats. In

addition, we show that meerkats carrying the MHC allele Susu-DRB\*13 were

initially more likely to develop clinical signs of TB, with the effect reversing

over the course of the study, followed by an increase in the frequency of

Susu-DRB\*13. Meerkats carrying Susu-DRB\*13 also showed slower progression to TB

signs and longer survival once signs of TB manifested. Lifetime reproductive

success reflected the resilience effect conferred by Susu-DRB\*13. Based on

several lines of evidence, we propose that rare-allele advantage or fluctuating

selection, rather than heterozygote advantage, drive our observation in this

longitudinally sampled wild mammal population.

© 2025. The Author(s).

DOI: 10.1038/s41559-025-02837-x

PMID: 40855227

**37. J Antibiot (Tokyo). 2025 Aug 25. doi: 10.1038/s41429-025-00862-3. Online ahead of print.**

Strategic design of a multi-tier database for class A β-lactamase BlaC variants

of M. tuberculosis: advancing the fight against antibacterial resistance.

Kumar KCA(1), Nair A(2)(3)(4), Sharma S(2), Singh D(2)(4), Yadav S(2), Bhimsaria

D(2)(5), Gupta S(6), Hazra S(7)(8).

Author information:

(1)Division of Data Analytics, Bioinformatics and Structural Biology, Yenepoya

Research Centre, Yenepoya University, Mangalore, India.

(2)Department of Biosciences and Bioengineering, Indian Institute of Technology

Roorkee, Roorkee, India.

(3)Centre for Nanotechnology, Indian Institute of Technology Roorkee, Roorkee,

India.

(4)Department of Physics, Indian Institute of Technology Roorkee, Roorkee,

India.

(5)Mehta Family School of Data Science and Artificial Intelligence, Indian

Institute of Technology, Roorkee, India.

(6)Division of Data Analytics, Bioinformatics and Structural Biology, Yenepoya

Research Centre, Yenepoya University, Mangalore, India. sebantigupta@gmail.com.

(7)Department of Biosciences and Bioengineering, Indian Institute of Technology

Roorkee, Roorkee, India. saugata.iitk@gmai.com.

(8)Centre for Nanotechnology, Indian Institute of Technology Roorkee, Roorkee,

India. saugata.iitk@gmai.com.

The escalating rise of antimicrobial resistance (AMR) casts a grave shadow over

global public health, making once manageable infections increasingly difficult

to treat. Despite advancements in combination chemotherapy for

multidrug-resistant (MDR) and extensively drug-resistant (XDR) Mycobacterium

tuberculosis (TB), this pathogen remains a formidable foe. TB is now the second

leading cause of death worldwide from infectious diseases, only surpassed by

COVID-19. It is the primary driver of AMR-related deaths, particularly among HIV

co-infected individuals. A significant challenge lies in TB's resistance to

β-lactam antibiotics, the most widely used class, comprising about 65% of global

antibiotic consumption. This resistance is driven by the bacterium's β-lactamase

enzyme (BlaC) production, which neutralizes the antibiotic by hydrolyzing the

β-lactam ring. Although BlaC remains susceptible to β-lactamase inhibitors

(MBIs) like sulbactam, tazobactam, and clavulanate, resistance mutations in

secondary catalytic sites pose an emerging threat, potentially undermining these

inhibitors. To combat this evolving challenge, a comprehensive study explored

BlaC's role in AMR. The research spanned six phases, from gene and protein

sequence analysis to dynamic protein modelling and mutational landscape

exploration. Homology modelling was employed to generate structures for all 40

BlaC variants, with stability assessed through Ramachandran plots. Drug-protein

interactions with six β-lactam agents and MBIs were investigated via automated

docking and simulation studies. These insights provide a deeper understanding of

BlaC-mediated resistance in TB and offer a promising foundation for future drug

development to address this global health crisis.

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Association.

DOI: 10.1038/s41429-025-00862-3

PMID: 40854973

**38. BMC Pediatr. 2025 Aug 25;25(1):647. doi: 10.1186/s12887-025-05554-3.**

Novel and optimized diagnostics for pediatric TB in endemic countries:

NOD-pedFEND study protocol.

Song R(#)(1), Bijker EM(#)(2)(3), Kisitu G(#)(4), Douglass E(#)(5), Nasinghe

E(6)(7), Basile FW(2), Khambati N(2), Penn-Nicholson A(8), Ruhwald M(8), Kim

S(9), Mudrak N(2), Dendukuri N(10), Ugarte-Gil C(11), Salgame P(#)(5), Alland

D(#)(12), Dorman SE(#)(13), Ellner J(#)(5), Joloba M(#)(6)(7), Kekitiinwa

A(#)(4); NOD-pedFEND consortium.

Collaborators: Muzorah GA, Ahimbisibwe G, Aloyo S, Ansiima S, Armstrong D, Arora

K, Babirye SR, Balwa H, Bashir K, Borkman A, Bugumirwa E, Caceres T, Calderon R,

Cavallini A, Cohen T, Vos M, Egere U, Eichberg C, Francia KGA, Graham SM, Haumba

G, Hom D, Indravudh PP, Kakyama F, Kalawa F, Kanyange A, Kasibante S, Kawwoya

NA, Kik SV, Koire M, Kyamulabi D, Lagos Y, Lovaton N, Lubega JP, Nabatanzi R,

Malobela A, Marais BJ, Matovu F, Mbekeka P, Menzies N, Mestanza F, Mirembe A,

Moron C, Mugabe RM, Mugabi B, Nabirye R, Nabisere A, Nabuduwa S, Nakagwa M,

Nakalanda BS, Nakayita G, Nakiyingi L, Namaganda R, Night C, Ninsiima G, Odongo

I, Olbrich L, Palmer M, Perez G, Post R, Rogers K, Schaaf HS, Schiller I,

Ssengooba W, Sweeney S, Tagoola A, Tufariello A, Turyamubona A, Upadhyay R,

Villa L, Wobudeya E, Xie Y, Yupanqui M, Zamudio C.

Author information:

(1)Oxford Vaccine Group, Department of Paediatrics, University of Oxford,

Oxford, UK. rinn.song@paediatrics.ox.ac.uk.

(2)Oxford Vaccine Group, Department of Paediatrics, University of Oxford,

Oxford, UK.

(3)Department of Paediatrics, Maastricht University Medical Centre, Mosakids

Children'S Hospital, Maastricht, the Netherlands.

(4)Baylor College of Medicine Children'S Foundation-Uganda, Kampala, Uganda.

(5)Division of Infectious Diseases, Center for Emerging Pathogens, New Jersey

Medical School, Rutgers University, Newark, NJ, USA.

(6)Department of Immunology and Molecular Biology, College of Health Sciences,

Makerere University, Kampala, Uganda.

(7)Integrated Biorepository of the H3africa Uganda, Kampala, Uganda.

(8)FIND, Geneva, Switzerland.

(9)Frontier Science Foundation, Brookline, MA, USA.

(10)Research Institute of the, Mcgill University Health Centre, Montreal, QC,

Canada.

(11)Universidad Peruana Cayetano Heredia, Lima, Peru.

(12)Public Health Research Institute, New Jersey Medical School, Rutgers

University, Newark, NJ, USA.

(13)Medical University of South Carolina, Charleston, SC, USA.

(#)Contributed equally

**BACKGROUND:** Pediatric tuberculosis is a major global public health challenge,

with reliable diagnosis being a main obstacle to identifying and treating

affected children. New and improved diagnostics, ideally on non-sputum samples,

are urgently required, especially in the most vulnerable group of children under

five years of age. Studies to date have been limited by small sample sizes and

few bacteriologically-confirmed cases. Here, we describe the study protocol of

the NIH-funded NOD-pedFEND study, which will be one of the largest diagnostic

studies to date of children at greatest risk of tuberculosis.

**METHODS:** In this prospective observational cohort study, we aim to evaluate

existing and novel diagnostic assays, including pathogen- and host-based tests

and combinations of tests. A consecutive cohort of children under five years of

age with signs and symptoms of tuberculosis is enrolled in Uganda and Peru. All

children undergo an extensive baseline workup with signs- and symptoms

recording, microbiological reference tests, chest X-ray and tuberculin skin test

for rigorous classification according to internationally recognized

microbiological, composite reference and strict standards. An array of samples

is collected for investigational tests. Follow-up visits are conducted at

2 weeks, 2 months and 6 months. A small cohort of healthy controls is enrolled

to evaluate the specificity of selected diagnostics. The study has been approved

by the relevant institutional review boards.

**DISCUSSION:** With this large cohort study of children under five years of age, we

aim to make an important contribution to the evaluation of new diagnostics for

pediatric tuberculosis. By establishing a comprehensive biorepository, the study

will also enable the assessment of novel tests as they become available during

and after the study.

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DOI: 10.1186/s12887-025-05554-3

PMCID: PMC12376364

PMID: 40851094 [Indexed for MEDLINE]

**39. mBio. 2025 Aug 25:e0095825. doi: 10.1128/mbio.00958-25. Online ahead of print.**

Experimental system enables studies of Mycobacterium tuberculosis during

aerogenic transmission.

Nuritdinov F(#)(1), Woo J(#)(1), Schmidt MJ(#)(2), Odjourian NM(1), Cristaldo

M(1), Dougher M(1), Antilus-Sainte R(1), Heldt T(2), Rhee K(3), Bourouiba L(2),

Gengenbacher M(1)(4).

Author information:

(1)Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, New

Jersey, USA.

(2)Fluids and Health Network, Institute for Medical Engineering and Science,

Massachusetts Institute of Technology, Cambridge, Massachusetts, USA.

(3)Division of Infectious Diseases, Weill Department of Medicine, Weill Cornell

Medical College, New York, New York, USA.

(4)Hackensack Meridian School of Medicine, Nutley, New Jersey, USA.

(#)Contributed equally

Tuberculosis, a persistent public health challenge worldwide, is transmitted

when exhaled Mycobacterium tuberculosis (Mtb) particles expelled from an

infected individual are inhaled by a susceptible person. To study the adaptation

of Mtb during transition between hosts, we developed a transmission simulation

system (TSS) that combines controlled pathogen aerosolization and measurement of

bioaerosol particle characteristics with in-flight sampling of Mtb and infection

of mice by nose-only exposure. Using scattered-light spectrometry, we

demonstrated that Mtb aerosol concentrations generated by the TSS better

represented human cough than the aerosol concentrations produced by a full-body

inhalation exposure system commonly used for Mtb infection of mice.

Additionally, the TSS deposited clinically relevant low doses of Mtb into murine

lungs with greater precision than the full-body inhalation exposure systems. The

TSS revealed a linear correlation between Mtb inoculum concentration and

pathogen deposition in murine lungs up to 200 colony-forming units. Higher

inoculum concentrations led to a reduction in total particle number, which

resulted in disproportionately lower pulmonary infection doses. Importantly, the

particle size distributions of Mtb-laden aerosols produced by the TSS mirrored

those of tuberculosis patient coughs, with 90% of culturable Mtb found in

particles with aerodynamic diameters below 3.3 µm. In conclusion, the TSS

represents a novel effective and precise translational platform enabling

detailed biophysical and molecular studies of Mtb transmission.

**IMPORTANCE:** Tuberculosis is transmitted when exhaled Mycobacterium tuberculosis

(Mtb)-laden microdroplets of an infected individual are inhaled by a susceptible

person. Historically, studies on Mtb transmission have focused mainly on

epidemiology due to the technical challenges in replicating the transmission

process effectively in a laboratory setting. In this study, we introduce a

transmission simulation system (TSS) that integrates controlled Mtb

aerosolization, biophysical aerosol particle measurements, in-flight Mtb

sampling, and aerosol infection of mice. The TSS generated Mtb bioaerosol

concentrations comparable to those produced by human coughs. These pathogen

droplets were accurately deposited in mouse lungs at low Mtb doses relevant to

human transmission. Notably, the distribution of Mtb among aerosol particles of

various sizes closely mirrored that found in the coughs of tuberculosis

patients. In summary, the TSS represents a novel tool for conducting molecular

studies of Mtb transmission through the air.

DOI: 10.1128/mbio.00958-25

PMID: 40853127

**40. Prep Biochem Biotechnol. 2025 Aug 25:1-11. doi: 10.1080/10826068.2025.2551369.**

**Online ahead of print.**

Scalable extracellular expression of tag-free MPT64 protein in E. coli via pelB

signal optimization: a step toward tuberculosis diagnostic antigen preparation.

Kusuma SAF(1), Fatinah Y(1), Fadhlillah M(2)(3), Parwati I(4), Rukayadi Y(5),

Subroto T(2)(3).

Author information:

(1)Department of Biology Pharmacy, Faculty of Pharmacy, Padjadjaran University,

Sumedang, West Java, Indonesia.

(2)Department of Chemistry, Faculty of Mathematics and Natural Sciences,

Padjadjaran University, Indonesia.

(3)Research Center of Molecular Biotechnology and Bioinformatics, Padjadjaran

University, Bandung, Indonesia.

(4)Clinical Pathology Department, Faculty of Medical, Padjadjaran University,

Indonesia.

(5)Department of Food Science, Faculty of Food Science and Technology,

Universiti Putra Malaysia, Serdang, Malaysia.

Tuberculosis (TB) remains a global health burden, requiring affordable and

scalable diagnostic tools. The MPT64 protein is a secreted biomarker specific to

Mycobacterium tuberculosis and holds promise for rapid antigen-based

diagnostics. However, existing recombinant expression systems often yield low

extracellular amounts, complicating purification and limiting downstream

application. This study aimed to optimize the extracellular, tag-free expression

of MPT64 protein in Escherichia coli by employing the pelB signal peptide in

combination with Response Surface Methodology (RSM). A Box-Behnken design was

used to analyze the interactive effects of rhamnose concentration, induction

timing, and medium composition. The optimal condition (4 mM rhamnose, 2-h

induction, and 1.8-fold medium enrichment) yielded 0.0293 mg/mL of extracellular

MPT64. The identity and antigenicity of the secreted protein were validated

using Sodium Dodecyl Sulfate Polyacrylamide Gel Electrophoresis (SDS-PAGE) and

lateral flow immunoassay (LFIA), respectively. This study demonstrates that

fine-tuning expression parameters can significantly enhance extracellular

protein yield, providing a cost-effective production strategy for MPT64-based TB

diagnostics and laying the foundation for future scalable diagnostic

development.

DOI: 10.1080/10826068.2025.2551369

PMID: 40852953

**41. Euro Surveill. 2025 Aug;30(34):2500633. doi:**

**10.2807/1560-7917.ES.2025.30.34.2500633.**

Increase in tuberculosis notification rates among newly arriving male Ukrainian

refugees to Norway, 2022 to 2024.

Nordstrand K(1), Berild JD(1).

Author information:

(1)Norwegian Institute of Public Health, Oslo, Norway.

The war in Ukraine has caused large population displacements. We report

increasing tuberculosis (TB) notification rates among Ukrainian refugees to

Norway detected through systematic screening upon arrival and driven by rates

among adult males. From 2022 to 2024, there were 73 TB notifications in

Ukrainians; incidence among Ukrainian men reached 248 per 100,000 in 2024. In 22

cases, isolated Mycobacterium tuberculosis were multidrug-resistant. Adequate TB

surveillance and control strategies are important to prevent TB outbreaks,

including multidrug-resistant TB, in Europe.

DOI: 10.2807/1560-7917.ES.2025.30.34.2500633

PMCID: PMC12397723

PMID: 40878702 [Indexed for MEDLINE]

**42. Pediatr Int. 2025 Jan-Dec;67(1):e70127. doi: 10.1111/ped.70127.**

An adolescent case of pancreatic tuberculosis after treatment of latent

tuberculosis infection.

Nakano Y(1)(2), Yamada K(2)(3), Suzuki K(2), Yasutomi-Sakai M(2), Takeuchi M(4),

Ohshima Y(2)(5).

Author information:

(1)Department of Pediatrics, Fukui Red Cross Hospital, Fukui City, Fukui, Japan.

(2)Department of Pediatrics, University of Fukui, Yoshida-gun, Fukui, Japan.

(3)Division of Infectious Disease, Department of Pediatrics, Hyogo Prefectural

Kobe Children's Hospital, Chuo-ku Kobe, Hyogo, Japan.

(4)Department of Pediatrics, National Hospital Organization Tsuruga Medical

Center, Tsuruga City, Fukui, Japan.

(5)Hyogo Prefectural Amagasaki General Medical Center, Amagasaki, Hyogo, Japan.

DOI: 10.1111/ped.70127

PMCID: PMC12392374

PMID: 40874505

**43. Vaccines (Basel). 2025 Aug 19;13(8):876. doi: 10.3390/vaccines13080876.**

BCG Vaccine-Induced Innate and Adaptive Pulmonary Immunity Correlating with

Protective Efficacy Against Mycobacterium tuberculosis in the Lungs.

Khanna M(1), Ramsay AJ(1).

Author information:

(1)Department of Microbiology, Immunology and Parasitology, Louisiana State

University Health Sciences Center, and the Louisiana Vaccine Center, New

Orleans, LA 70112, USA.

**Background/Objectives:** Effective prophylaxis for Mycobacterium tuberculosis

(Mtb) requires greater understanding of immune correlates of protection. With

renewed interest in BCG as an Mtb vaccine, particularly via the intravenous (IV)

route, our objective was to characterize both innate and adaptive immune

correlates of vaccine-induced pulmonary immunity as potential biomarkers for

protective efficacy in a murine model of Mtb infection. **Methods:** Mice were given

BCG via different routes and some boosted with recombinant virus constructs

encoding Mtb Ag85B. Responding innate lymphoid cell (ILC) populations, T cells

and B cells were analyzed by fluorescence activated cell sorting (FACS) for

surface markers and by intracellular cytokine staining or antibody ELISPOT. Some

immunized mice were challenged with aerosolized Mtb and monitored for bacterial

growth in the lungs and spleen. **Results:** BCG given IV, but not intranasally or

subcutaneously, resulted in marked increases in IFNγ expression at 72 h by

pulmonary CD49+ NK cells, CD69+ ILC1, and two ILC3 populations, NCR-ILC3 and LTi

cells, the latter also producing IL-22. Pulmonary ILC2 populations in these mice

had significantly increased IL-13 expression at 24 h compared to the other

routes. Interestingly, high levels of NK cells and ILC1 expressing IFNγ and/or

TNFα were sustained at 8 wk, with sustained expression of IL-17A by pulmonary

NCR-ILC3 and pronounced tissue-resident and effector memory CD4+ and CD8+ T cell

responses. Intranasal boosting with Ad-Ag85B enhanced these T cell responses and

generated Mtb-specific pulmonary IgA and IgG B cells, correlating with

significantly reduced bacterial loads following Mtb challenge. **Conclusions:** BCG

given IV primed for both early and persistent pulmonary ILC1/ILC3 responses of a

predominantly Th1/Th17-type profile along with local Mtb-specific memory T cell

and B cell populations, correlating with enhanced protective efficacy. These are

worthy of further study as compartmentalized biomarkers for effective

vaccine-induced local immunity against Mtb.

DOI: 10.3390/vaccines13080876

PMCID: PMC12389847

PMID: 40872961

**44. Vaccines (Basel). 2025 Aug 15;13(8):868. doi: 10.3390/vaccines13080868.**

Modelling the Impact of Vaccination and Other Intervention Strategies on

Asymptomatic and Symptomatic Tuberculosis Transmission and Control in Thailand.

Kuddus MA(1), Tithi SK(1), Theparod T(2).

Author information:

(1)Department of Mathematics, University of Rajshahi, Rajshahi 6205, Bangladesh.

(2)Department of Mathematics, Mahasarakham University, Maha Sarakham 44150,

Thailand.

**Background:** Tuberculosis (TB) remains a major global health challenge, including

in Thailand, where both asymptomatic and symptomatic cases sustain transmission.

The disease burden increases treatment complexity and mortality, requiring

integrated care and coordinated policies. **Methods**: We developed a deterministic

compartmental model to examine the transmission dynamics of TB in Thailand,

incorporating both latent and active stages of infection, as well as vaccination

coverage. The model was calibrated using national TB incidence data, and

sensitivity analysis revealed that the TB transmission rate was the most

influential parameter affecting the basic reproduction number (R0). We evaluated

the impact of several intervention strategies, including increased treatment

coverage for latent and active TB infections and improved vaccination rates.

**Results:** Our analysis indicates that among the single interventions, scaling up

effective treatment for latent TB infections produced the greatest reduction in

asymptomatic and symptomatic cases, while enhanced treatment for active TB cases

was second most effective for reducing both asymptomatic and symptomatic cases.

Importantly, our results indicate that combining multiple interventions yields

significantly greater reductions in overall TB incidence than any single

approach alone. Our findings suggest that a modest investment in integrated TB

control can substantially reduce TB transmission and disease burden in Thailand.

However, complete eradication of TB would require a comprehensive and sustained

investment to achieve near-universal coverage of both preventive and curative

strategies. **Conclusions:** TB remains a significant public health threat in

Thailand. Targeted interventions and integrated strategies are key to reducing

disease burden and improving treatment outcomes.

DOI: 10.3390/vaccines13080868

PMCID: PMC12389990

PMID: 40872953

**45. Pathogens. 2025 Aug 20;14(8):824. doi: 10.3390/pathogens14080824.**

Human Tuberculosis in Migrant and Autocthonous Patients: A Ten-Year

Single-Centre Experience.

Soriano IG(1), Romero M(1)(2), Gascón I(3), Solves V(3), Pascual R(1)(2),

Wikman-Jorgensen PE(1)(2).

Author information:

(1)Infectious Diseases Unit, Department of Internal Medicine, Hospital General

Universitario de Elda-FISABIO, 03600 Elda, Spain.

(2)Department of Clinical Medicine, Miguel Hernández University, 03550 San Juan

de Alicante, Spain.

(3)Microbiology Unit, Clinical Analysis Department, Hospital General

Universitario de Elda, 03600 Elda, Spain.

In recent years, migratory movements have increased. This study aimed to compare

tuberculosis cases in migrant and autochthonous patients. We conducted a

retrospective analytical cohort study of patients diagnosed with tuberculosis in

the Elda Health District (Alicante, Spain) between 2013 and 2023. Of the 98

patients analyzed, 28 (29.6%) were migrants, predominantly male (65%), with a

mean age of 35.6 years. Pulmonary tuberculosis was present in 82% of patients in

both groups, and nine cases of drug-resistant tuberculosis were identified. No

significant differences were observed between groups in treatment cure rates,

mortality, or hospitalization. Unfavourable outcomes-a composite endpoint

comprising mortality, treatment failure, and loss to follow-up-were more

frequent in males and in patients with elevated C-reactive protein (CRP) levels

(p = 0.033) or a higher CRP/albumin ratio. Migrants accounted for a substantial

proportion of total TB cases and tended to be younger, with fewer comorbidities

and lower rates of substance use. They showed a non-significant trend toward

higher loss to follow-up and drug resistance. Overall, unfavourable outcomes

were associated with elevated CRP levels and the CRP/albumin ratio.

DOI: 10.3390/pathogens14080824

PMCID: PMC12389354

PMID: 40872333 [Indexed for MEDLINE]

**46. Pathogens. 2025 Aug 11;14(8):802. doi: 10.3390/pathogens14080802.**

Mycobacterium tuberculosis Modulates the Expansion of Terminally Exhausted

CD4(+) and CD8(+) T-Cells in Individuals with HIV-TB Co-Infection.

Sharma K(1), Sharma A(2), Arora SK(1).

Author information:

(1)Molecular Immunology Laboratory, Department of Immunopathology, Post Graduate

Institute of Medical Education & Research (PGIMER), Chandigarh 160012, India.

(2)Department of Internal Medicine, Post Graduate Institute of Medical Education

& Research (PGIMER), Chandigarh 160012, India.

**INTRODUCTION:** Mycobacterium tuberculosis (Mtb), the most common co-infection

among people living with HIV (PLWH), aggravates the associated morbidity and

mortality in these individuals; however, the immune-modulatory role of Mtb in

the pathogenesis of HIV infection remains incompletely understood.

**METHODS:** We investigated the role of Mtb infection in regulating adaptive immune

responses with reference to the expression of five immune checkpoint molecules

(ICMs) in co-infected individuals in a cross-sectional study conducted on

treatment-naïve human cohorts from North India, including PLWH, people with Mtb

infection, people with HIV-Mtb co-infection, and healthy volunteers as controls.

**RESULTS:** The data revealed a significantly increased gene expression of TIM-3 (p

= 0.0058), LAG-3 (p < 0.0001), PD-1 (p = 0.0090), and CTLA-4 (p = 0.0008). It

also revealed a higher frequency of CD4+ and CD8+ T-cells surface-expressing

TIM-3+, CTLA-4+, LAG-3+. Finally, it showed cells co-expressing two ICMs

together (p < 0.05) in individuals with HIV-Mtb co-infection as compared to HIV

mono-infected ones. Interestingly, the frequency of these cells correlated

inversely with the absolute CD4+ T-cell count and positively with the plasma

viral load (p < 0.05), indicating direct association with HIV disease

progression.

**CONCLUSIONS:** These findings suggest that Mtb co-infection exacerbates immune

exhaustion in co-infected individuals. Targeting ICMs with pharmacological

immune checkpoint inhibitors (ICIs) offers a promising approach for better

clinical management of co-infected individuals.

DOI: 10.3390/pathogens14080802

PMCID: PMC12389345

PMID: 40872312 [Indexed for MEDLINE]

**47. Pathogens. 2025 Aug 5;14(8):772. doi: 10.3390/pathogens14080772.**

Multisystemic Tuberculosis Masquerading as Aggressive Cardiac Tumor Causing

Budd-Chiari Syndrome Disseminated to the Brain Resulting in Death of a

Six-Year-Old Boy.

Al-Akhali ES(1)(2), Alshoabi SA(3), Muslem HF(4), Alhazmi FH(3), Alsaedi AF(3),

Alsultan KD(3), Alzain AF(3), Omer AM(3), Elzaki M(3), Hamid AM(5).

Author information:

(1)Department of Radiology, Al Anwar Medical Hospital, Hail 55424, Saudi Arabia.

(2)Department of Radiology, Advanced AlRazi Diagnostic Center, Sana'a 999101,

Yemen.

(3)Department of Diagnostic Radiology, College of Applied Medical Sciences,

Taibah University, Al-Madinah Al-Munawwarah 42353, Saudi Arabia.

(4)Department of Internal Medicine, Dr. Suliman Al Habib Hospital Altakhasosi,

Riyadh 12344, Saudi Arabia.

(5)Radiology Department, Rush University Medical Group, Chicago, IL 60612, USA.

Tuberculosis (TB) is an ancient and re-emerging granulomatous infectious disease

that continues to challenge public health. Early diagnosis and prompt effective

treatment are crucial for preventing disease progression and reducing both

morbidity and mortality. These steps play a vital role in infection control and

in lowering death rates at both individual and population levels. Although

diagnostic methods have improved sufficiently in recent decades, TB can still

present with ambiguous laboratory and imaging features. This ambiguity can lead

to diagnostic pitfalls and potentially disastrous outcomes due to delayed

diagnosis. In this article, we present a case of TB that was difficult to

diagnose. The disease had invaded the mediastinum, right atrium, right coronary

artery, and inferior vena cava (IVC), resulting in Budd-Chiari syndrome. This

rare presentation created clinical, laboratory, and radiological confusion,

resulting in a diagnostic dilemma that ultimately led to open cardiac surgery.

The patient initially presented with progressive shortness of breath on exertion

and fatigue, which suggested possible heart disease. This suspicion was

reinforced by computed tomography (CT) imaging, which showed infiltrative mass

lesions predominantly in the right side of the heart, invading the right

coronary artery and IVC, with imaging features mimicking angiosarcoma. Although

laboratory findings revealed an exudative effusion with lymphocyte predominance

and elevated adenosine deaminase (ADA), the Gram stain was negative for

bacteria, and an acid-fast bacilli (AFB) smear was also negative. These findings

contributed to diagnostic uncertainty and delayed the confirmation of TB. Open

surgery with excisional biopsy and histopathological analysis ultimately

confirmed TB. We conclude that TB should not be ruled out solely based on

negative Mycobacterium bacteria in pericardial effusion or AFB smear. TB can

mimic aggressive tumors such as angiosarcoma or lymphoma with invasion of the

surrounding tissues and blood vessels. Awareness of the clinical presentation,

imaging findings, and potential diagnostic pitfalls of TB is essential,

especially in endemic regions.

DOI: 10.3390/pathogens14080772

PMCID: PMC12388990

PMID: 40872282 [Indexed for MEDLINE]

**48. Pathogens. 2025 Jul 28;14(8):741. doi: 10.3390/pathogens14080741.**

Advancing Extrapulmonary Tuberculosis Diagnosis: Potential of MPT64

Immunochemistry-Based Antigen Detection Test in a High-TB, Low-HIV Endemic

Setting.

Wali A(1)(2), Safdar N(3), Ambreen A(4), Loya A(5), Mustafa T(1)(6).

Author information:

(1)Centre for International Health, Department of Global Public Health and

Primary Care, University of Bergen, Arstadveien 21, 5009 Bergen, Norway.

(2)Department of Health, Government of Balochistan, Civil Secretariat, Zarghoon

Road, Quetta 87300, Pakistan.

(3)Interactive Research and Development, Level 10, One George Street, Singapore

049145, Singapore.

(4)Department of Microbiology, Gulab Devi Teaching Hospital, Lahore 05441,

Pakistan.

(5)Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research

Center, 7A Block R-3 MA Johar Town, Lahore 54000, Pakistan.

(6)Department of Thoracic Medicine, Haukeland University Hospital, Bergen,

Haukelandsveien 22, 5009 Bergen, Norway.

Extrapulmonary tuberculosis (EPTB) remains diagnostically challenging due to its

paucibacillary nature and variable presentation. Xpert and culture are limited

in EPTB diagnosis due to sampling challenges, low sensitivity, and long

turnaround times. This study evaluated the performance of the MPT64 antigen

detection test for diagnosing EPTB, particularly tuberculous lymphadenitis

(TBLN) and tuberculous pleuritis (TBP), in a high-TB, low-HIV setting. Conducted

at Gulab-Devi Hospital, Lahore, Pakistan, this study evaluated the MPT64 test's

performance against conventional diagnostic methods, including culture,

histopathology, and the Xpert MTB/RIF assay. Lymph node biopsies were collected,

and cell blocks were made from aspirated pleural fluid from patients clinically

presumed to have EPTB. Of 338 patients, 318 (94%) were diagnosed with EPTB. For

TBLN, MPT64 demonstrated higher sensitivity (84%) than Xpert (48%); for TBP, the

sensitivity was 51% versus 7%, respectively. Among histopathology-confirmed TBLN

cases, MPT64 outperformed both culture and Xpert (85% vs. 58% and 47%). Due to

the low number of non-TB cases, specificity could not be reliably assessed. The

MPT64 test shows promise as a rapid, sensitive diagnostic tool for EPTB,

particularly TBLN, in routine settings. While sensitivity is notably superior to

Xpert, further studies are needed to evaluate its specificity and broader

diagnostic utility.

DOI: 10.3390/pathogens14080741

PMCID: PMC12388923

PMID: 40872251 [Indexed for MEDLINE]

**49. Pathogens. 2025 Jul 27;14(8):740. doi: 10.3390/pathogens14080740.**

Risk Factors for Latent Tuberculosis Identified Using Epidemiological

Investigation in Congregate Settings of Gyeongsan City, Republic of Korea

(2014-2023).

Park S(1), Lee K(2).

Author information:

(1)Health and Public Administration Department, Republic Health Center,

Gyeongsan 38616, Gyeongsangbuk-do, Republic of Korea.

(2)Department of Preventive Medicine, Dongguk University College of Medicine,

Gyeongju 38066, Gyeongsangbuk-do, Republic of Korea.

Latent tuberculosis infection (LTBI) remains an important public health issue,

as individuals can harbor Mycobacterium tuberculosis without symptoms and later

develop active disease. This study aimed to assess the prevalence and risk

factors associated with LTBI positivity among tuberculosis (TB) contacts in

congregate settings in Gyeongsan City, the Republic of Korea (ROK), from 2014 to

2023. A total of 213 index cases and 3666 contacts were analyzed using data from

the Korea Tuberculosis Infection Control System (KTB-NET). Overall, 20.7% of

contacts tested positive for LTBI, with the highest rates observed among

contacts aged ≥65 years (50.4%) and in healthcare facilities (34.8%). Binary

logistic regression analyses revealed that age ≥65 years (OR: 2.93; 95% CI:

1.95-4.39; p < 0.001), social welfare facilities (OR: 2.75; 95% CI: 2.10-3.58; p

< 0.001), workplaces (OR: 2.42; 95% CI: 1.88-3.10; p < 0.001), and healthcare

facilities (OR: 3.42; 95% CI: 2.63-4.43; p < 0.001) were significantly

associated with increased LTBI risk. These findings highlight the importance of

targeted interventions and prevention strategies focused on older adults and

high-risk groups to prevent future TB outbreaks by reducing the burden of LTBI.

DOI: 10.3390/pathogens14080740

PMCID: PMC12389638

PMID: 40872250 [Indexed for MEDLINE]

**50. Diagnostics (Basel). 2025 Aug 11;15(16):2008. doi: 10.3390/diagnostics15162008.**

Ultrasonography and Biomarkers in the Diagnostic Evaluation of Peritoneal

Tuberculosis: A Case Series Analysis.

Putra AD(1), Purwoto G(1), Sachi Y(1), Suhendar CW(1), Nugroho I(1), Saidah

I(1), Wirasugianto J(1), Amelia(1), Syariatin L(1), Lukas GA(1).

Author information:

(1)Division of Gynecologic Oncology, Department of Obstetrics and Gynecology,

Cipto Mangunkusumo Hospital, Central Jakarta 10430, Indonesia.

**Objectives:** This study aims to describe the ultrasound findings and biomarker

profiles (CA-125, HE4, CEA, ADA, and IGRA) in confirmed cases of peritoneal

tuberculosis (PTB) and to discuss their relevance in clinical evaluation.

**Methods:** This is a retrospective study utilizing data from 12 female subjects

with a confirmed PTB diagnosis at Cipto Mangunkusumo Hospital and Hermina Depok

Hospital between 2018 and 2023. Data were extracted from medical records.

Biomarker levels were measured using standardized assays in a single accredited

laboratory. Ultrasonography was performed using the Mindray Resona 7 system.

**Results:** The mean age was 33.0 ± 9.7 years. Ultrasonography identified

significant features of PTB, such as hydrosalpinx 7 (58.3%), adhesions 6 (50%),

ascites 7 (58.3%), cystic/mass-like lesions 4 (33.3%), and involvement of the

rectosigmoid colon and small bowel 2 (16.6%). CA-125 levels were elevated (mean:

484.25 U/mL), and HE4 was high in 41.6% of cases (mean: 66.8 pmol/L). CEA levels

remained low (mean: 1.725 ng/mL), and ADA levels were elevated in all patients

(mean: 45.8 U/L). IGRA testing yielded a 75% positivity rate, with one patient

converting from negative to positive after a month**. Conclusions:** Ultrasound

remains a valuable imaging modality for identifying characteristic features of

PTB, particularly hydrosalpinx and ascites. Elevated CA-125 and ADA, alongside

IGRA results, may support clinical suspicion and help guide diagnosis in

settings where invasive procedures are limited.

DOI: 10.3390/diagnostics15162008

PMCID: PMC12385388

PMID: 40870860

**51. Int J Environ Res Public Health. 2025 Aug 14;22(8):1272. doi:**

**10.3390/ijerph22081272.**

Assessment of the Syndemic Relationship Between Individual, Social, and

Structural Determinants of Tuberculosis Among People Living in Johannesburg,

South Africa.

Tanyanyiwa FT(1), Van Wyk RH(1), Setswe KG(2)(3).

Author information:

(1)Department of Environmental Health, Faculty of Health Sciences, University of

Johannesburg, Johannesburg 2006, South Africa.

(2)Implementation Research Division, Aurum Institute, Johannesburg 2193, South

Africa.

(3)Department of Health Studies, University of South Africa, Pretoria 0003,

South Africa.

Tuberculosis (TB) remains a critical public health issue in Johannesburg, South

Africa, driven by a complex interplay of individual, social, and structural

factors. This study assessed the syndemic relationship between these

determinants to understand their collective impact on TB burden and treatment

outcomes. A cross-sectional survey was conducted among TB patients attending

selected clinics, examining behavioural risks (e.g., smoking, alcohol use, HIV

co-infection), social conditions (poverty, overcrowding, stigma), and structural

challenges (access to healthcare, migration status). The results revealed a

significant co-occurrence of TB and HIV (56.1%), alongside high rates of smoking

(33.1%) and alcohol use (45.2%). Unemployment (50.2%), inadequate housing, and

limited healthcare access, particularly for undocumented migrants (26.2%), were

also prominent. Factor analysis demonstrated a syndemic interaction between

behavioural and social determinants, underscoring the compounded vulnerability

of affected populations. The findings highlight the necessity of integrating

medical interventions with social and structural reforms. Recommendations

include TB-HIV co-management, substance abuse programmes, improved housing, and

inclusive healthcare access. A multisectoral approach addressing both health and

socioeconomic inequalities is critical for comprehensive TB control in urban

South African contexts.

DOI: 10.3390/ijerph22081272

PMCID: PMC12386250

PMID: 40869857 [Indexed for MEDLINE]

**52. J Clin Med. 2025 Aug 11;14(16):5681. doi: 10.3390/jcm14165681.**

Tuberculosis in Pregnant Women After COVID-19: Features of Prevention,

Diagnosis, and Treatment (Narrative Review).

Starshinova A(1)(2), Belyaeva E(1), Irtyuga O(2), Sefiyeva G(2), Mitrofanova

L(2), Makarov I(2), Makarova T(2), Kulpina A(1)(2), Kudlay D(3)(4)(5).

Author information:

(1)Department of Mathematics and Computer Science, St-Petersburg State

University, St. Petersburg 199034, Russia.

(2)Almazov National Medical Research Centre, St. Petersburg 197341, Russia.

(3)Department of Pharmacology, Institute of Pharmacy, I.M. Sechenov First Moscow

State Medical University, Moscow 119991, Russia.

(4)Institute of Immunology FMBA of Russia, Moscow 115522, Russia.

(5)Department of Pharmacognosy and Industrial Pharmacy, Faculty of Fundamental

Medicine, Lomonosov Moscow State University, Moscow 119991, Russia.

Tuberculosis remains a serious infectious disease that causes over 1.3 million

deaths annually. Following the COVID-19 pandemic, the global incidence of

tuberculosis has increased to 10.8 million cases. Pregnant women represent a

particularly vulnerable population requiring tailored approaches to the

prevention, diagnosis, and treatment of tuberculosis. SARS-CoV-2 infection may

have impacted existing clinical protocols. Implementing updated methods of

tuberculosis prevention, diagnosis, and treatment in pregnant women could help

reduce adverse maternal and fetal outcomes. The aim of this review was to

explore potential modifications in tuberculosis management among pregnant women

in the post-COVID-19 era, including co-infection with SARS-CoV-2. Methods: A

review was conducted, incorporating a systematic literature search across major

international databases, including Medline, PubMed, Web of Science, Scopus, and

Google Scholar. The search covered publications released between December 2019

and September 2024 and used targeted keywords such as "COVID-19" OR

"SARS-CoV-2", "tuberculosis" OR "TB" OR "latent tuberculosis infection" OR

"pulmonary tuberculosis", and "pregnancy" OR "pregnant women". Results: Pregnant

women living with HIV are at increased risk of developing tuberculosis, which

can negatively affect both maternal and perinatal outcomes. Screening for

tuberculosis is recommended for all HIV-positive pregnant women, even in the

absence of clinical symptoms. Notably, immunological testing before and during

pregnancy facilitates the timely and safe detection of tuberculosis infection,

enabling preventive and therapeutic interventions during any stage of gestation

and the early postpartum period, for the benefit of both mother and child.

Drug-drug interactions play a significant role in tuberculosis management, both

among anti-tuberculosis agents and with medications for comorbid conditions.

Current knowledge of the pharmacokinetics and pharmacodynamics of

antituberculosis agents, coupled with therapeutic drug monitoring, supports the

development of individualized and effective treatment regimens, which are

particularly critical for pregnant patients. Recommendations for managing

tuberculosis in pregnant women after COVID-19 infection include measuring

D-dimer levels, performing echocardiography, and consulting cardiologists to

prevent treatment-related complications. Conclusions: Pregnant women represent a

distinct subgroup of tuberculosis patients requiring individualized management.

Changes observed in tuberculosis progression and treatment responses in pregnant

women before and after SARS-CoV-2 infection should inform therapeutic choices,

especially in cases of drug-resistant tuberculosis treated with bedaquiline.

COVID-19 has been associated with increased cardiovascular risk, which may

heighten the likelihood of adverse drug reactions in this population, especially

given the limited therapeutic options. Further research is required to assess

the long-term outcomes of latent tuberculosis infection in pregnant women and to

evaluate the safety and efficacy of novel regimens for drug-resistant TB during

pregnancy.

DOI: 10.3390/jcm14165681

PMCID: PMC12386941

PMID: 40869505

**53. Curr Issues Mol Biol. 2025 Jul 23;47(8):585. doi: 10.3390/cimb47080585.**

New Tool Against Tuberculosis: The Potential of the LAMP Lateral Flow Assay in

Resource-Limited Settings.

Rosas-Diaz M(1), Palacios-Reyes C(2), Godinez-Aguilar R(3), Escalante-Bautista

D(4), Alfaro Hernández L(5), Juarez-Islas AP(6), Segundo-Ibañez P(6),

Salas-Cuevas G(6), Olvera-Serrano Á(6), Hernandez-Martinez JC(1), Ramos-Garcia

VH(1), Garcia Oropesa EM(1), Flores-García O(6), Galvez-Romero JL(7), León

Burgoa G(8), Nolasco-Quiroga M(6).

Author information:

(1)Molecular Biology Laboratory, Multidisciplinary Academic Unit Reynosa-Aztlan

Reynosa, Autonomous University of Tamaulipas, Ciudad Victoria 88740, Tamaulipas,

Mexico.

(2)Department of Medical Sciences, Division of Health Sciences, University of

Guanajuato, Campus Leon, León de los Aldama 37000, Guanajuato, Mexico.

(3)Direction and Division of Research, Hospital Juárez de México, Av. Instituto

Politécnico Nacional 5160, Magdalena de las Salinas, Gustavo A. Madero, Mexico

City 07760, Mexico.

(4)Human Genetics Medical Research Unit, Pediatric Hospital, National Medical

Center of the Mexican Institute for Segurity (IMSS), Cuauhtémoc, Mexico City

06720, Mexico.

(5)Laboratory of Cytomics of Childhood, Biomedical Research Center of the East,

Puebla Delegation, Mexican Institute of Social Security, Atlixco 74360, Puebla,

Mexico.

(6)Molecular Biology Laboratory of Hospital Clinic Huauchinango, Institute of

Social Security and Services for State Workers, Huauchinango 73160, Puebla,

Mexico.

(7)Department of Research of the Regional Hospital ISSSTE of Puebla, Boulevard

14 Sur 4336, Colonia Jardines de San Manuel, Puebla 72570, Mexico.

(8)Public Health Laboratory of Puebla, Secretary of Health Mexico, Puebla

772490, Mexico.

Tuberculosis (TB) is a global public health issue requiring early and accurate

diagnosis. The loop-mediated isothermal amplification (LAMP) assay is a

promising alternative recommended by the WHO for the initial diagnosis of

pulmonary TB, particularly in resource-limited settings. This study evaluated

the sensitivity and specificity of a commercial LAMP assay for TB detection

using 198 samples from different countries including Mexico. The LAMP assay

results were compared to the results of standard tests: AFB smear microscopy,

cell culture, and Xpert PCR. Across all samples, LAMP showed a sensitivity of

96.20% and a specificity of 84.61%. When compared specifically to "true

positives" and "true negatives" (defined by the consistency across the standard

tests), LAMP demonstrated 100% sensitivity and 92.30% specificity. For context,

the sensitivity of AFB smear microscopy against the culture and Xpert tests was

79.04%. A significant finding was that the LAMP test detected a high percentage

(92.5%) of samples found positive by the culture and Xpert tests but negative by

the AFB smear, highlighting its ability to identify cases missed by traditional

microscopy. This study concluded that the LAMP assay is a sensitive and specific

tool for TB diagnosis with potential for rapid and accurate diagnosis,

especially in resource-limited areas.

DOI: 10.3390/cimb47080585

PMCID: PMC12384488

PMID: 40864739

**54. Front Vet Sci. 2025 Aug 13;12:1609526. doi: 10.3389/fvets.2025.1609526.**

**eCollection 2025.**

Bovine tuberculosis source attribution using decision tree analysis: breakdown

investigations in Italy (2022-2023).

Tamba M(1), Galletti G(1), Loda D(2), Salvato S(1), De Nardi M(3), Boniotti

MB(2).

Author information:

(1)Epidemiology Unit, Istituto Zooprofilattico Sperimentale della Lombardia e

dell'Emilia Romagna "B. Ubertini", Bologna, Italy.

(2)National Reference Laboratory for Bovine Tuberculosis, Department of Animal

Health, Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia

Romagna "B. Ubertini", Brescia, Italy.

(3)Department of Veterinary Medical Sciences (DIMEVET), Alma Mater Studiorum -

University of Bologna, Ozzano dell'Emilia, Italy.

In this study, we present an overview of 348 Bovine Tuberculosis (bTB)

breakdowns reported in Italy between January 2022 and December 2023, and

declared resolved between January 2022 and February 2025. The main objective of

this study is to investigate the most probable sources of these bTB breakdowns

using decision tree analysis, and to compare the findings with conclusions drawn

by official veterinarians. Most of the studied breakdowns (332; 95.4%) involved

cattle herds only, 11 (3.1%) involved water buffalo herds only, and five (1.4%)

involved multiple species. bTB was primarily detected in beef herds (82.8%),

while mixed and dairy herds represented 10.3 and 6.9% of the breakdowns,

respectively. In half of the breakdowns, the number of reactors was four or

fewer. We also collected genotype data for 268 Mycobacterium tuberculosis

complex isolates from 191 (54.9%) different breakdowns. M. bovis (255 isolates;

95.1%) came from 180 (94.2%) breakdowns, showing wide genetic variability. M.

caprae (13 isolates; 4.9%) came from 11 (5.8%) breakdowns. Finally, we

investigated the probable sources of infection, considering the five most

frequently proposed sources of bTB breakdowns: (i) residual infection; (ii)

introduction of infected cattle from other herds; (iii) sharing of pastures with

infected herds; (iv) contiguous spread from infected neighboring herds; and (v)

interaction with wildlife reservoirs. For each source, a decision tree was

developed, and a likelihood of infection was assigned to each end node of the

trees. The analysis identified residual infection (11.2%) as the most frequent

source of bTB breakdowns, followed by sharing of pastures (10.9%) and

interaction with wildlife (7.2%). The introduction of infected cattle and

contiguous spread from infected neighboring herds were identified as less

relevant sources. These tools allowed us to identify a likely source of

infection in about 26% of cases. The results of our study, although based on

scientific criteria, showed poor agreement with the conclusions of the

veterinary officers who conducted the breakdown investigations in the field. In

our opinion, these tools, when added to the "classic" investigation

methodologies, should improve their effectiveness in identifying sources of

infection in bTB breakdowns in Italy, supporting the eradication of this

zoonotic disease.

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DOI: 10.3389/fvets.2025.1609526

PMCID: PMC12380583

PMID: 40881636

**55. Cureus. 2025 Jul 28;17(7):e88918. doi: 10.7759/cureus.88918. eCollection 2025**

**Jul.**

Barriers to Care Leading to Fatal Consequences: A Case of Tuberculosis Sepsis

Amid Policy Change.

Khawar Z(1), Chakkera M(1), Malik D(2), Slim J(3).

Author information:

(1)Internal Medicine, Saint Michael's Medical Center, Newark, USA.

(2)Internal Medicine, St. Mary's General Hospital, Passaic, USA.

(3)Infectious Diseases, Saint Michael's Medical Center, Newark, USA.

Mycobacterium tuberculosis is an acid-fast bacterium with a diverse range of

clinical manifestations and is considered rare in Western countries.

Tuberculosis (TB) remains a global health concern and can pose several

challenges in diagnosis and treatment. Paired with changing immigration

policies, immigrant populations can face several barriers to healthcare. This

case illustrates the impact of immigration policy on clinical outcomes and how

government policies can act as a barrier to care. We present a case of a

26-year-old Guatemalan man with no known past medical history who came to the

emergency department hemodynamically unstable with the presentation of abdominal

perforation. He was urgently taken for an exploratory laparotomy, which revealed

two perforations in the terminal ileum, extensive fibrinous exudate in the

peritoneal cavity, and significant lymphadenopathy in the mesentery and

retroperitoneum. The specimens collected intraoperatively were sent for

evaluation and showed necrotizing granulomatous inflammation with transmural

necrosis, and mesenteric lymph node biopsy revealed necrotizing granulomatous

lymphadenitis, findings consistent with TB lymphadenitis. A sputum acid-fast

bacilli (AFB) test further confirmed Mycobacterium tuberculosis. Given the

concern for disseminated TB and ongoing ventilator and pressor support, this

case required a multidisciplinary critical care course. The patient was started

on antimycobacterial therapy with plans to transition to RIPE (rifampin,

isoniazid, pyrazinamide, and ethambutol) therapy plus vitamin B6. The patients'

hospital course was further complicated by loculated ascites with peritonitis

and necrotizing pneumonia. Despite aggressive multidisciplinary medical therapy,

the patient ultimately expired. The treatment of sepsis due to disseminated TB

depends heavily on the ability to identify the causal infection, in addition to

providing hemodynamic and organ support. The research stressing the timeliness

of treatment and its impact on mortality in sepsis and miliary TB is well

documented across medical literature. In this case, it is critical to analyze

the political climate that may have prevented the patient from presenting to a

healthcare provider when he first experienced symptoms.

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**56. Pediatr Infect Dis J. 2025 Jul 25. doi: 10.1097/INF.0000000000004928. Online**

**ahead of print.**

Endobronchial Tuberculosis With Cavitation in Early Infancy: A Diagnostic

Challenge.

Ekemen C(1), Avcu G(1), Arslan A(1), Ozer EC(1), Kartal Ozturk G(2), Sahbudak

Bal Z(1).

Author information:

(1)Division of Infectious Disease, Department of Pediatrics, Medical School of

Ege University, Izmir, Turkey.

(2)Division of Pulmonology, Department of Pediatrics, Medical School of Ege

University, Izmir, Turkey.

DOI: 10.1097/INF.0000000000004928

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**57. Trop Med Infect Dis. 2025 Aug 20;10(8):235. doi: 10.3390/tropicalmed10080235.**

Screening for Latent Tuberculosis Across Chronic Kidney Disease Stages Using

Interferon-Gamma Release Assay: Findings from a National Infectious Disease

Institute in Thailand.

Pongpirul W(1), Pongpirul K(2)(3)(4), Tiabrat V(1), Muennoo K(1), Prasithsirikul

W(1).

Author information:

(1)Bamrasnaradura Infectious Diseases Institute, Department of Disease Control,

Ministry of Public Health, Nonthaburi 11000, Thailand.

(2)Center of Excellence in Preventive and Integrative Medicine, Faculty of

Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

(3)Department of Infection Biology & Microbiomes, Faculty of Health and Life

Sciences, University of Liverpool, Liverpool L69 3GE, UK.

(4)Clinical Research Center, Bumrungrad International Hospital, Bangkok 10110,

Thailand.

**BACKGROUND:** Latent tuberculosis infection (LTBI) is a major global health

concern, particularly among individuals with chronic kidney disease (CKD), who

are at increased risk of reactivation due to impaired immunity and frequent

exposure to immunosuppressive therapies. Despite growing reliance on

interferon-gamma release assays (IGRAs) such as QuantiFERON-TB Gold In-Tube

(QFT-GIT) in BCG-vaccinated populations, data on IGRA performance across CKD

stages remain limited in resource-limited settings.

**OBJECTIVE:** To determine the prevalence of LTBI and indeterminate IGRA results

across CKD stages in a Thai population and assess the clinical utility of IGRA

in this context.

**MATERIALS AND METHODS:** We conducted a cross-sectional study among 785 Thai

adults receiving care at a national infectious disease institute, including

diabetes clinic patients, hospital staff, and individuals on hemodialysis. Each

participant underwent QFT-GIT testing, and the CKD stage was classified using

the estimated glomerular filtration rate (eGFR) closest prior to testing.

**RESULTS:** Overall IGRA positivity was 22.2%, peaking in CKD stage G3 (31.6%) and

declining in stage G5 (11.0%), where indeterminate results were also highest

(6.8%).

**LIMITATIONS:** Single-center design and lack of confirmatory testing may limit

generalizability.

**CONCLUSIONS:** IGRA performance is reliable in early-to-moderate CKD but less so

in advanced stages. LTBI is prevalent in CKD stages G2-G4, supporting

stage-specific approaches to LTBI screening and caution against overreliance on

IGRA in advanced renal impairment.

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PMCID: PMC12390336

PMID: 40864138

**58. Trop Med Infect Dis. 2025 Aug 12;10(8):226. doi: 10.3390/tropicalmed10080226.**

Unmasking the Determinants of Loss to Follow-Up in Pulmonary Tuberculosis: A

Study in Selangor, Malaysia.

Mohd Ghazali S(1), Cheong KC(2), Md Nadzri MN(1), Mohd Ghazali N(1), Cheng

LM(1), Ahmad LCRQ(1), Kamarudin MK(1), Ahmad NAR(1), Zulkifli AA(1), Ling CY(1),

Ruslan Q(1), Singh S(1), Gill BS(1), Razali A(3), Md Iderus NH(1).

Author information:

(1)Institute for Medical Research, National Institutes of Health, Ministry of

Health, Shah Alam 40170, Malaysia.

(2)Sector for Biostatistics and Data Repository, National Institutes of Health,

Ministry of Health, Shah Alam 40170, Malaysia.

(3)Disease Control Division, Ministry of Health Malaysia, Putrajaya 62590,

Malaysia.

Adherence to the 6-month tuberculosis (TB) treatment regimen is challenging due

to its duration and side effects, with various factors influencing patient

compliance. A retrospective cross-sectional study was conducted among newly

diagnosed pulmonary TB (pTB) patients in Selangor, Malaysia, undergoing

treatment in government primary care clinics and hospitals. Patients who were

lost to follow-up (LTFU) within the first six months were determined by

reviewing patient records and the national TB registry. Logistic regression

analysis identified sociodemographic and clinical factors associated with LTFU.

Of the 699 pTB patients, 55 (7.9%) were lost to follow-up. Factors significantly

associated with LTFU included age (higher in 25-44-year-olds, adjusted odds

ratio (aOR): 2.83), unmarried status (aOR: 2.17), lower education level (aOR:

6.13), being a smoker (aOR: 2.65), and unawareness of TB diagnosis (aOR: 38.14).

A significant interaction was found between education level and awareness of

diagnosis, with unawareness having a stronger association with LTFU among

higher-educated patients. Young adults, those with a lower education level,

unmarried individuals, smokers, and those unaware of their TB diagnosis are at

higher risk of LTFU. These factors can be used for rapid risk assessment.

Intensive counselling and health education at treatment initiation, particularly

for at-risk patients, are crucial for preventing LTFU.

DOI: 10.3390/tropicalmed10080226

PMCID: PMC12390508

PMID: 40864129

**59. Trop Med Infect Dis. 2025 Jul 30;10(8):214. doi: 10.3390/tropicalmed10080214.**

Tuberculosis-Related Knowledge, Attitudes, and Practices Among Healthcare

Workers in Atlantic Canada: A Descriptive Study.

Oh HJ(1), Law MA(2), Shamputa IC(3).

Author information:

(1)Faculty of Medicine, Dalhousie Medicine New Brunswick, Saint John, NB E2L

4L5, Canada.

(2)Department of Psychology, University of New Brunswick, Saint John, NB E2L

4L5, Canada.

(3)Department of Nursing and Health Sciences, University of New Brunswick, Saint

John, NB E2L 4L5, Canada.

**INTRODUCTION:** Despite the key role of healthcare workers (HCWs) in tuberculosis

(TB) prevention and control, there is a lack of regional data on their

knowledge, attitudes, and practices (KAPs) regarding the disease in Atlantic

Canada.

**OBJECTIVES:** To assess the KAPs of HCWs and identify targets for educational

interventions to enhance TB care and control.

**METHODS:** A cross-sectional study was conducted among HCWs in Atlantic Canada

aged ≥19 years from October 2023 to February 2024. Participants were recruited

via multiple channels such as social media, collegiate email lists, and snowball

sampling. Survey data were collected using an online platform and analyzed using

IBM SPSS Statistics v29. KAPs were assessed using Likert-type scales and

internal consistency was evaluated using Cronbach's alpha.

**RESULTS:** A total of 157 HCWs participated in this study (age range: 19 to 69

years); most were women (n = 145, 92%), born in Canada (n = 134, 85.4%), with

nearly three-quarters (n = 115, 73.2%) who had never lived outside of Canada.

Study participants demonstrated moderately high knowledge (M = 29.32, SD = 3.25)

and positive attitudes (M = 3.87, SD = 0.37) towards TB and strong practices (M

= 4.24, SD = 0.69) in TB care; however, gaps were identified in HCW abilities to

recognize less common TB symptoms (e.g., rash and nausea), as well as

inconsistent practices in ventilation and pre-treatment initiation. Internal

consistency analysis indicated suboptimal reliability across all three KAP

domains, with Cronbach's alpha values falling below 0.7, thwarting further

planned analyses.

**CONCLUSIONS:** This study found overall moderate-to-strong TB-related KAPs among

HCWs in Atlantic Canada; however, critical gaps in knowledge and practice were

noted. This new information can now guide future educational initiatives and

targeted training to enhance TB preparedness and ensure equitable care for

patients in the region.

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PMCID: PMC12390285

PMID: 40864117

**60. Open Forum Infect Dis. 2025 Jul 18;12(8):ofaf425. doi: 10.1093/ofid/ofaf425.**

**eCollection 2025 Aug.**

Factors Predictive of Early Discontinuation of Preventive Treatment in Children

With Household Exposure to Multidrug-resistant Tuberculosis.

Duong T(1), Brigden J(1), Purchase SE(2), Martinson NA(3)(4), Fairlie L(5),

Staples S(6), Patel F(5), Sabet N(3), Layton C(1), Wilkinson T(7), Schaaf HS(2),

Seddon JA(2)(8), Hesseling AC(2).

Author information:

(1)Institute of Clinical Trials and Methodology, Faculty of Population Health

Sciences, University College London, London, UK.

(2)Desmond Tutu TB Centre, Department of Paediatrics and Child Health,

Stellenbosch University, Cape Town, South Africa.

(3)Perinatal HIV Research Unit, University of the Witwatersrand, Johannesburg,

South Africa.

(4)Center for Tuberculosis Research, Department of Medicine, Johns Hopkins

University School of Medicine, Baltimore, Maryland, USA.

(5)Wits RHI, Faculty of Health Sciences, University of the Witwatersrand,

Johannesburg, South Africa.

(6)Tuberculosis & HIV Investigative Network, Research Department, Durban, South

Africa.

(7)Health Economics Unit, University of Cape Town, Cape Town, South Africa.

(8)Department of Infectious Disease, Imperial College London, London, UK.

**BACKGROUND:** The World Health Organization recommended levofloxacin for

tuberculosis (TB) preventive treatment for child and adult contacts of

multidrug-resistant TB.

**METHOD:** TB-CHAMP (ISRCTN92634082) was a double-blind community-based multisite

randomized placebo-controlled trial assessing levofloxacin as preventive

treatment in children with household exposure to adults with microbiologically

confirmed multidrug-resistant TB in South Africa. Households were randomized 1:1

to 24 weeks of daily levofloxacin (adult scored 250-mg tablets) versus placebo.

Treatment adherence was ascertained through pill counts and treatment cards.

Competing risk methods were used to assess factors associated with early

treatment discontinuation for nonclinical reasons before achieving ≥80% of

allocated doses (adequate treatment).

**RESULTS:** Among 911 of 922 children included in analysis, 90% were younger than 5

years of age. Overall, 765 (84%) of children achieved adequate treatment, 135

(15%) discontinued treatment early, and 11 (1%) had not achieved adequate

treatment by the end-of-treatment period. Sixty-four (7%) children stopped for

clinical reasons and 71 (8%) for nonclinical reasons, with similar proportions

across treatment groups. Baseline factors associated with early treatment

discontinuation for nonclinical reasons were previous receipt of

herbal/traditional medicine (subhazard ratio 3.08; 95% confidence interval,

1.69-5.59; P < .001), and caregivers reporting difficulties administering

medication (subhazard ratio 2.73; 1.11-6.71; P = .029). Children with poor

treatment adherence by week 4 were more likely to subsequently stop treatment

early for nonclinical reasons (subhazard ratio 2.72; 1.06-6.97; P = .037).

**CONCLUSIONS:** Adherence to the 250-mg levofloxacin formulation was good among

young children on preventive TB therapy. Adherence support for children and

caregivers, and addressing early signs of poor adherence, may enhance treatment

completion.

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Infectious Diseases Society of America.

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PMID: 40874184

**61. Clin Kidney J. 2025 Jun 19;18(7):sfaf197. doi: 10.1093/ckj/sfaf197. eCollection 2025 Jul.**

Screening for latent tuberculosis infection in patients with chronic kidney

disease: a review of evidence and current practice in the UK.

Sturman J(1)(2), Baharani J(2), Ashman J(2), Harper L(2)(3), Cunningham AF(1),

Dedicoat M(4), O'Shea MK(1)(4).

Author information:

(1)Department of Immunology and Immunotherapy, School of Infection, Inflammation

and Immunology, College of Medicine and Health, University of Birmingham,

Birmingham, UK.

(2)Department of Renal Medicine, University Hospitals Birmingham NHS Foundation

Trust, Birmingham, UK.

(3)Department of Applied Health Sciences, School of Health Sciences, University

of Birmingham, Birmingham, UK.

(4)Department of Infectious Diseases, University Hospitals Birmingham NHS

Foundation Trust, Birmingham, UK.

Tuberculosis (TB) and chronic kidney disease (CKD) represent an extant local and

global syndemic, with TB incidence rates in the UK end-stage renal failure

population far surpassing those of the general population in endemic countries.

Patients with CKD generally have latent TB reactivation, rather than de novo

infection, which presents with atypical, non-pulmonary presentations leading to

late diagnosis, poorer outcomes and a high risk of widespread transmission

through haemodialysis units. There is therefore a need to consider latent TB

infection screening in the CKD population. However, there is widespread

variation in local screening practices in the UK due to the challenge of

diagnosing latent TB in CKD, and the absence of robust evidence-based

guidelines. There is also concern that although a screening programme may have

significant public health benefit, it may cause harm to the individual patient

through adverse effects of treatment. In this review, we present the current

evidence for latent TB infection screening in CKD, including the evidence of

benefit and harm to the individual and the public. We also review current

practices in the UK and present survey data from renal units in England

demonstrating the diversity of policies currently in place. We advocate

screening for latent TB in all CKD patients commencing dialysis and we highlight

the pressing research questions that need to be urgently answered to help move

towards a cohesive national policy to help drive evidence-based consistent care.

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**62. Front Immunol. 2025 Aug 12;16:1608769. doi: 10.3389/fimmu.2025.1608769.**

**eCollection 2025.**

Susceptibility to and severity of tuberculosis infection in mice depends upon

MHC-II-determined level of activation-inhibition balance in CD4 T-cells.

Logunova N(1), Kapina M(1), Kriukova V(2), Britanova O(3)(4)(5), Majorov K(1),

Linge I(1), Apt A(1).

Author information:

(1)Laboratory for Immunogenetics, Central Research Tuberculosis Institute,

Moscow, Russia.

(2)Institute of Clinical Molecular Biology, Christian-Albrechts-University of

Kiel, Kiel, Germany.

(3)Immunoengineering Laboratory, Pirogov Russian National Research Medical

University, Moscow, Russia.

(4)Abu Dhabi Stem Cells Center, Abu Dhabi,, United Arab Emirates.

(5)Department of Genomics of Adaptive Immunity, Shemyakin - Ovchinnikov

Institute of Bioorganic Chemistry, Moscow, Russia.

Previously we have shown that H2-congenic recombinant mice of the B6.I-9.3

(H2-Ab1 j) strain are significantly more susceptible to tuberculosis (TB)

infection compared to their C57BL/6 (B6, H2-A b) ancestors. Impaired TB control

was characterized by decreased selection and maintenance of CD4+ T-cells, their

profoundly narrower TCR repertoires, and a disproportionally enlarged neutrophil

population. All phenotypes were expressed before TB infection, thus reflecting

the steady state of the immune system and providing the basis of true genetic TB

susceptibility. We anticipated that the differences in parameters of

pre-infection immune homeostasis would seriously influence development of

specific immune responses shortly after mycobacterial invasion and affect TB

defense thereafter. In this study, we report on the dynamic phenotypes of CD4+

T-cells responding to infection which differ profoundly between mice bearing

different MHC-II alleles. First, during post-challenge week 3, despite identical

lung mycobacterial load, mice carrying the "resistant" H2-A b allele recruited

significantly more mycobacteria-specific, IFN-γ-producing CD4+ T-cells to their

lungs compared to H2-Ab1 j allele carriers. Second, during a few months post

challenge, B6 mice were able to control both the size of the IFN-γ-producing

CD4+ T-cell population and the total proportion of activated CD4+ T-cells at

levels significantly lower than those in B6.I-9.3 mice. Finally, in

TB-susceptible mice, a higher proportion of CD4+ T-cells expressed both

activation-associated and immune inhibition (checkpoint) markers, accompanied by

functional CD4+ T-cell exhaustion at late stages of infection. Together, these

observations suggest that suboptimal pre-infection MHC-II-dependent shifts in

immune homeostasis affect both early and late immune reactions against TB.

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PMID: 40873577 [Indexed for MEDLINE]

**63. Front Immunol. 2025 Aug 12;16:1665988. doi: 10.3389/fimmu.2025.1665988.**

**eCollection 2025.**

Editorial: Immune response in tuberculosis with comorbidities or coinfections.

Gomes-Silva A(1), Babu S(2)(3), Cavalcanti Rolla V(1).

Author information:

(1)Laboratório de Pesquisa Clínica em Micobacterioses, Instituto Nacional de

Infectologia Evandro Chagas, FIOCRUZ, Rio de Janeiro, Brazil.

(2)Department of ICER, National Institutes of Health-National Institute of

Allergy and Infectious Diseases-International Center for Excellence in Research,

Chennai, India.

(3)Laboratory of Parasitic Diseases, National Institutes of Allergy and

Infectious Diseases, National Institutes of Health, Bethesda, MD, United States.

Comment on

 Editorial on the Research Topic Immune response in tuberculosis with

comorbidities or coinfections.

DOI: 10.3389/fimmu.2025.1665988

PMCID: PMC12378162

PMID: 40873560

**64. Infect Disord Drug Targets. 2025 Aug 22. doi:**

**10.2174/0118715265384910250721042045. Online ahead of print.**

Primary Tuberculous Intramuscular Abscess in a Diabetic Elderly Male: An Unusual

Case Report.

Dinkar A(1)(2), Singh J(3)(4), Patwa AK(3), Kumar S(5), Atam I(6).

Author information:

(1)Department of Microbiology, Sanjay Gandhi Postgraduate Institute of Medical

Sciences, Lucknow, Uttar Pradesh, India.

(2)Department of Microbiology, Institute of Medical Sciences, Banaras Hindu

University, Varanasi, Uttar Pradesh, India.

(3)Department of General Medicine, King George's Medical University, Lucknow,

Uttar Pradesh, India.

(4)Department of General Medicine, Institute of Medical Sciences, Banaras Hindu

University, Varanasi, India.

(5)Department of Radiodiagnosis, King George's Medical University, Lucknow,

Uttar Pradesh, India.

(6)Department of Physiology, King George`s Medical University, Lucknow, Uttar

Pradesh, India.

**BACKGROUND:** Tuberculosis (TB) primarily affects the lungs, but extrapulmonary

manifestations, such as musculoskeletal TB, account for 15-20% of cases.

Isolated intramuscular TB abscesses are exceedingly rare cases of extrapulmonary

TB. Predisposing factors, such as diabetes mellitus, immunosuppression, and

advanced age, increase the risk of such atypical presentations. This report

presents a rare case of a primary tuberculous intramuscular abscess in an

elderly diabetic male, emphasizing diagnostic challenges and the importance of a

multidisciplinary approach.

**CASE PRESENTATION:** A 63-year-old male with uncontrolled type 2 diabetes

presented with a 2-month history of right thigh pain and progressive swelling.

Examination revealed an 8×9 cm, nontender, firm lump in the right thigh with

normal overlying skin. Imaging with 3T MRI showed a multilobulated fluid

collection in the thigh's upper third region, predominantly in the adductor and

anterior compartments, with surrounding muscle edema and multiple enlarged

inguinal lymph nodes. Histo-pathological examination of drained material

revealed caseating granulomas with Langhans giant cells, consistent with

tuberculosis. CBNAAT confirmed rifampicin-sensitive Mycobacterium tuberculosis.

The patient was diagnosed with a primary tuberculous abscess and initiated on a

6-month antituberculosis therapy. He showed significant clinical improvement at

the 1-month follow-up and successfully completed his 6-month ATT without any

intolerance.

**CONCLUSION:** This case underscores the importance of considering TB in atypical

presentations, particularly in endemic regions and high-risk populations. Prompt

diagnosis through advanced imaging, histopathology, molecular testing, and

appropriate surgical and pharmacological interventions is crit-ical for optimal

outcomes in such rare presentations.

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epub@benthamscience.net.

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PMID: 40873170

**65. Int J Environ Res Public Health. 2025 Jul 31;22(8):1209. doi:**

**10.3390/ijerph22081209.**

Determinants of Non-Adherence to Anti-Tuberculosis Treatment in a Public Primary

Healthcare Clinic in South Africa: Improving the Quality of Long-Term Care.

Katende-Kyenda LN(1).

Author information:

(1)Department of Internal Medicine and Pharmacology, Faculty of Medicine and

Health Sciences, Walter Sisulu University, Sissons Street, Fortgale, Mthatha

5117, Eastern Cape, South Africa.

**BACKGROUND:** Non-adherence to anti-tuberculosis treatment remains a major

obstacle to increasing tuberculosis treatment success rates and enhancing

healthcare expenditure. The aim of this study was to identify determinants

contributing to non-adherence to anti-tuberculosis treatment in a public primary

healthcare clinic in South Africa.

**METHOD:** A cross-sectional study was carried out to collect data from 65

participants using face-to-face interviews with a structured questionnaire. Data

were analyzed using SPSS.

**RESULTS:** Of the 65 participants interviewed, 41 (63.08%) were males and 24

(36.92%) were females. A total of 45 (69.23%) were adherents and 20 (30.77%)

were non-adherents. Gender was the major predictor of non-adherence with more

males committed to treatment than females with a significant association (X2 =

65.00 and p of <0.001).

**CONCLUSIONS:** The major contributing factors to non-adherence were long

dis-tances to the clinics, a lack of family support, and unemployment.

Comprehensive programs addressing these multifactorial factors are needed for

successful treatment and eradication of tuberculosis.

DOI: 10.3390/ijerph22081209

PMCID: PMC12386246

PMID: 40869795 [Indexed for MEDLINE]

**66. Trop Med Infect Dis. 2025 Jul 24;10(8):206. doi: 10.3390/tropicalmed10080206.**

Evaluating the Gaps in the Diagnosis and Treatment in Extra-Pulmonary

Tuberculosis Patients Under National Tuberculosis Elimination Programme (NTEP)

Guidelines: A Multicentric Cohort Study.

Sinha S(1), Titiyal R(1), Mohapatra PR(2), Palvai RK(3), Kar I(2), Mishra B(2),

Ajayababu A(1), Sinha A(1), Bhuniya S(2), Pandey S(4).

Author information:

(1)Department of Medicine, All India Institute of Medical Sciences, Ansari

Nagar, New Delhi 110029, India.

(2)Department of Pulmonary Medicine & Critical Care, AII India Institute of

Medical Sciences, Bhubaneswar 751019, India.

(3)Government General & Chest Hospital, Hyderabad 500013, India.

(4)Department of Biostatistics, All India Institute of Medical Sciences, Ansari

Nagar, New Delhi 110029, India.

Extra-pulmonary tuberculosis (EPTB) can affect any organ of the body, producing

a wide variety of clinical manifestations that make the diagnosis and treatment

of EPTB challenging. The optimum treatment varies depending on the site of EPTB,

its severity, and response to treatment. There is often uncertainty about the

best management practices, with a significant departure from national

guidelines. This study aims to identify gaps and barriers in adhering to the

national guidelines for the diagnosis and treatment of EPTB. We included 433

patients having EPTB and followed up at predefined intervals of 2 months, 6

months, 9 months, and 12 months. Questionnaire-based interviews of the treating

physician and the patients in different departments were conducted. For

confirmatory diagnosis, heavy dependence on clinical-radiological diagnosis

without microbiological support was observed, which is a deviation from National

Tuberculosis Elimination Programme (NTEP) guidelines and raises concerns about

the potential for misdiagnosis and overtreatment. Apart from patient delays,

long health system delays in EPTB were observed. The median patient delay,

health system delay, and total treatment delay times were 4.2, 4, and 10.1

weeks, respectively. To enhance EPTB diagnosis and management, there is a

pressing need for improved access to microbiological testing, enhanced physician

training on adherence to NTEP guidelines, and greater utilisation of imaging and

histopathological techniques.

DOI: 10.3390/tropicalmed10080206

PMCID: PMC12390147

PMID: 40864109

**67. Neurol Int. 2025 Aug 2;17(8):119. doi: 10.3390/neurolint17080119.**

Characterization of QuantiFERON-TB-Plus Results in Patients with Tuberculosis

Infection and Multiple Sclerosis.

Petruccioli E(1), Prosperini L(2), Ruggieri S(2), Vanini V(1)(3), Salmi A(1),

Cuzzi G(1), Galgani S(2), Haggiag S(2), Tortorella C(2), Parisi G(4), D'Agostino

A(4), Gualano G(5), Palmieri F(5), Gasperini C(2), Goletti D(1).

Author information:

(1)Translational Research Unit, National Institute for Infectious Diseases

Lazzaro Spallanzani-IRCCS, 00149 Rome, Italy.

(2)Department of Neurosciences, San Camillo Forlanini Hospital, 00152 Rome,

Italy.

(3)Unità Operativa Semplice (UOS) Professioni Sanitarie Tecniche, National

Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, 00149 Rome, Italy.

(4)Department of Clinical Microbiology and Virology, San Camillo Forlanini

Hospital, 00152 Rome, Italy.

(5)Respiratory Infectious Diseases Unit, National Institute for Infectious

Diseases Lazzaro Spallanzani-IRCCS, 00149 Rome, Italy.

**BACKGROUND:** Disease-modifying drugs (DMDs) for multiple sclerosis (MS) slightly

increase the risk of tuberculosis (TB) disease. The QuantiFERON-TB-Plus

(QFT-Plus) test is approved for TB infection (TBI) screening. Currently, there

are no data available regarding the characterization of QFT-Plus response in

patients with MS.

**OBJECTIVES:** This study aimed to compare the magnitude of QFT-Plus responses

between patients with MS and TBI (MS-TBI) and TBI subjects without MS

(NON-MS-TBI). Additionally, discordant responses to TB1/TB2 stimulation were

documented. Results were evaluated considering demographic and clinical data,

particularly the impact of DMDs and the type of TB exposure.

**METHODS:** Patients with MS (N = 810) were screened for TBI (2018-2023). Thirty

(3.7%) had an MS-TBI diagnosis, and 20 were recruited for the study. As a

control group, we enrolled 106 NON-MS-TBI.

**RESULTS:** MS-TBI showed significantly lower IFN-γ production in response to TB1

(p = 0.01) and TB2 stimulation (p = 0.02) compared to NON-MS-TBI. The 30% of TB2

results of MS-TBI fell into the QFT-Plus grey zone (0.2-0.7 IU/mL). Only 7% of

NON-MS-TBI showed this profile (p = 0.002).

**CONCLUSIONS:** MS-TBI had a lower QFT-Plus response and more borderline results

compared to NON-MS-TBI. Future studies should clarify the significance of the

borderline results in this vulnerable population to improve QFT-Plus accuracy

regarding sensitivity, specificity, and TB prediction.

DOI: 10.3390/neurolint17080119

PMCID: PMC12389123

PMID: 40863988

**68. Infect Dis Rep. 2025 Aug 6;17(4):96. doi: 10.3390/idr17040096.**

Scrofuloderma, an Old Acquaintance: A Case Report and Literature Review.

Lozada-Ramos H(1)(2), Daza-Arana JE(3).

Author information:

(1)Medicine Program, Faculty of Health, Universidad Santiago de Cali, Palmira

763532, Colombia.

(2)Doctoral Program in Infectious Diseases, Universidad de Santander-UDES,

Bucaramanga 680003, Colombia.

(3)Physiotherapy Program, Faculty of Health, Universidad Santiago de Cali, Cali

760035, Colombia.

Scrofuloderma, a cutaneous manifestation of tuberculosis, is a rare but

clinically significant form of mycobacterial infection. It typically results

from the local spread of Mycobacterium tuberculosis from an infected lymph node

or bone area to the overlying skin. This disease is mainly characterized by

chronic granulomatous inflammation, leading to skin ulcers and abscesses. Due to

its nonspecific clinical presentation, scrofuloderma can mimic various

dermatological conditions, making its diagnosis particularly challenging. This

case report presents the clinical course of a patient who was positive for the

Human Immunodeficiency Virus (HIV) with a diagnosis of scrofuloderma, managed at

a tertiary healthcare center, with follow-up before and after treatment. A

literature review was also made, highlighting the importance of maintaining a

high index of clinical suspicion and utilizing appropriate diagnostic methods to

ensure timely diagnosis.

DOI: 10.3390/idr17040096

PMCID: PMC12386262

PMID: 40863258

**69. Biomedica. 2025 Aug 11;45(3):423-435. doi: 10.7705/biomedica.7664.**

Prevalence and characterization of human immunodeficiency virus coinfection in

patients hospitalized with tuberculosis in a reference hospital in Bogotá.

[Article in English, Spanish]

Puentes-Ariza GC(1), Meléndez-Rhenals S(2), Nocua-Báez LC(1), Páez-Ardila H(3).

Author information:

(1)Departamento de Medicina Interna, Facultad de Medicina, Universidad Nacional

de Colombia, Bogotá, D. C., Colombia.

(2)Departamento de Medicina Interna, Facultad de Medicina, Universidad Nacional

de Colombia, Bogotá, D. C., Colombia; Servicio de Medicina Interna, Hospital

Universitario Nacional de Colombia, Corporación Salud UN, Bogotá, D.C.,

Colombia.

(3)Servicio de Infectología, Hospital Simón Bolívar, Bogotá, D.C., Colombia.

Introducción. La tuberculosis es la principal causa de muerte en los pacientes

con infección por el virus de la inmunodeficiencia humana. La coinfección de

Mycobacterium tuberculosis y HIV es muy frecuente. Objetivo. Establecer la

prevalencia de la infección por HIV en pacientes hospitalizados con

tuberculosis, y determinar sus características y desenlaces. Materiales y

métodos. Se realizó un estudio retrospectivo, de corte transversal, en pacientes

con tuberculosis -pulmonar o extrapulmonar- y coinfección por HIV,

hospitalizados en una institución de referencia de Bogotá entre el 2019 y el

2021. Resultados. En el grupo de los 102 pacientes con tuberculosis, la

prevalencia de infección por HIV fue del 52,3% (54). Entre estos 54, 24

pacientes (44,4%) tuvieron confirmación microbiológica o histopatológica de la

tuberculosis y, 19 (35,2 %), infección por VIH de novo. En los 54 coinfectados,

la mediana de la edad fue de 38 años (RIC: 29-42). El 79,6 % (43/54) fueron

hombres. La mediana del número de linfocitos T CD4+ fue de 59 células/μl (RIC:

32-120), y el 72,2 % (39/54) tenía menos de 200 células/μl. El 31,4 % (17/54) de

los pacientes con antecedente de infección por HIV recibía terapia

antirretroviral. En cuanto a la forma clínica, la tuberculosis fue pulmonar en

el 51,9 % (28/54) y extrapulmonar en el 48,1 % (26/54) de los pacientes. La

tuberculosis extrapulmonar fue meníngea (29,6 %), miliar (12,9 %), pleural (3,7

%) y peritoneal (3,7 %). Hubo 33,3 % de mortalidad intrahospitalaria, asociada

con el número de linfocitos T CD4+ (p < 0,05), el diagnóstico de novo de HIV (p

< 0,04) y la presencia de tuberculosis meníngea (p < 0,03). Conclusión. La

coinfección de Mycobacterium tuberculosis y HIV es frecuente y se relaciona con

una inmunosupresión avanzada, por lo que debe hacerse una búsqueda activa de la

infección con HIV en estos casos. La tuberculosis meníngea fue la forma

extrapulmonar más frecuente y se asoció con mortalidad.

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PMID: 40865109 [Indexed for MEDLINE]

**70. Cureus. 2025 Jul 23;17(7):e88572. doi: 10.7759/cureus.88572. eCollection 2025**

**Jul.**

Tuberculous Meningitis Complicated by Communicating Hydrocephalus and Lacunar

Infarcts: A Case Report.

Varghese RK(1), Mittapalli V(2), Chikkana G(2).

Author information:

(1)General Medicine, Ahalia Group, Abu Dhabi, ARE.

(2)Neurology, Ahalia Group, Abu Dhabi, ARE.

Tuberculous meningitis (TBM) is a life-threatening form of central nervous

system tuberculosis (CNS-TB) that often presents with diagnostic and therapeutic

challenges, especially in the absence of early microbiological confirmation, and

is often associated with complications. We report the case of a previously

healthy 32-year-old female who presented with a short history of fever,

headache, and altered mental status. Initial cerebrospinal fluid (CSF) analysis

revealed a profile consistent with TBM, though microbiological studies were

negative. MRI findings showed meningeal enhancement and vasculitic changes. The

patient experienced a rapid neurological decline with signs of raised

intracranial pressure, necessitating external ventricular drainage and later

ventriculoperitoneal (VP) shunting. She also developed hyponatremia likely

secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH),

and subsequent imaging revealed multiple lacunar infarcts suggestive of

vasculitis-related ischemic injury. CSF culture later confirmed Mycobacterium

tuberculosis. The patient responded favorably to empirical anti-tuberculous

therapy (ATT), adjunctive corticosteroids, and multidisciplinary supportive

care. She made a significant neurological recovery and was discharged ambulant

with minimal assistance. This report underscores the importance of early

clinical recognition, prompt empirical therapy, and timely neurosurgical

intervention in TBM to reduce morbidity, even when initial laboratory

confirmation is lacking. Multidisciplinary involvement, and proactive

complication management including that which covers hydrocephalus and

hyponatremia, are critical to improving outcomes.

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PMID: 40861613

**71. Front Pediatr. 2025 Aug 11;13:1638167. doi: 10.3389/fped.2025.1638167.**

**eCollection 2025.**

Young lungs cared enough? India's frontiers in diagnosing pediatric TB.

Thomas SV(1), Rajendran P(1), Shanmugam S(1).

Author information:

(1)Department of Bacteriology, National Institute for Research in Tuberculosis-

ICMR, Chennai, India.

This review provides an insight into pediatric tuberculosis (TB) diagnosis in

India. Significant challenges still exist in the accurate diagnosis of pediatric

TB due to the paucibacillary status of the bacilli and the nonspecific clinical

symptoms. Despite advancements in newer diagnostics that allow for rapid

identification of TB and detection of drug resistance in children, their

sensitivity is compromised due to these challenges. It is crucial to consider

that children may not always expectorate sputum, further complicating the

diagnostic process. Testing multiple samples, like aspirates, bronchoalveolar

lavages, stool, urine, saliva, and swabs, may improve sensitivity. However, the

efficacy of using these samples for pediatric TB diagnosis requires extensive

research to validate their accuracy and reliability. This is crucial, especially

in countries like India, which bears a high burden of TB cases, making the need

for novel diagnostic approaches even more pressing. This need for innovative

diagnostic approaches is particularly important in countries like India, which

bears a high burden of TB cases. Collaborative efforts between researchers,

healthcare providers, and policymakers are essential to drive innovation and

progress toward achieving the END-TB goal. In this review, we have included

studies and case reports published over a decade by utilizing scientific

databases like PubMed, Scopus, and Google Scholar, and a set of key search terms

including "pediatric TB in India", and "pediatric TB diagnosis".

© 2025 Thomas, Rajendran and Shanmugam.

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PMCID: PMC12375632

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**72. GMS Infect Dis. 2025 Jul 11;13:Doc03. doi: 10.3205/id000093. eCollection 2025.**

Cartridge-based nucleic amplification (CBNAAT)/GeneXpert test as a diagnostic

modality for the detection of genital tuberculosis in women with infertility.

Shaozae CK(1), Rai Y(1), Jaiswal N(2), Jais MB(1).

Author information:

(1)Department of Microbiology, Lady Hardinge Medical College and Associated SSK

and KSC Hospitals, New Delhi, India.

(2)Department of Obstetrics and Gynaecology, Lady Hardinge Medical College and

Associated SSK and KSC Hospitals, New Delhi, India.

**BACKGROUND:** Genital tuberculosis (GTB) is a significant etiological factor of

infertility in developing countries such as India; however, it is frequently

undiagnosed due to its asymptomatic nature and a lack of standardised protocols.

This study aimed to compare the diagnostic efficacy of GeneXpert (CBNAAT) with

Ziehl-Neelsen (ZN) staining, Mycobacterial Growth Indicator Tube (MGIT) liquid

culture and histopathological examination (HPE). Additionally, the occurrence of

GTB in infertile women aged between 18 and 45 years was also determined.

**METHODS:** The study comprised 200 infertile women with suspected GTB. Endometrial

biopsy samples were collected aseptically and subjected to ZN staining, MGIT

liquid culture, GeneXpert testing and HPE and the results were analysed and

compared. MGIT was considered the gold standard test in accordance with National

TB Elimination Programme (NTEP) recommendations.

**RESULTS:** There were 164 (82%) cases of primary infertility, and 36 (18%) cases

of secondary infertility. Out of the 200 samples of endometrial biopsy (EB)

specimens, the GeneXpert test detected two positive findings (1%), ZN staining

detected two positive results (1%), and MGIT liquid culture as well as HPE

detected one positive result (0.5%). GeneXpert demonstrated a sensitivity of

100% (confidence interval (CI) 2.50-100.00%), a specificity of 99.5% (CI

97.23-99.99%), a positive predictive value (PPV) of 50% (CI 12.40-87.60%), and a

negative predictive value (NPV) of 100% (CI 98.15-100.00%), with liquid culture

as reference. A significant agreement was found between the diagnostic

procedures of MGIT and GeneXpert, with a kappa value of 0.66 and a p-value of

0.047 (significant p-value <0.05).

**CONCLUSION:** The present study is among the few that has utilised GeneXpert to

aid in the diagnosis of female genital tuberculosis (FGTB). GeneXpert, being

much faster and more feasible than conventional methods such as culture, could

be incorporated into the standard evaluation of GTB.

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PMID: 40860964

**73. J Clin Exp Hepatol. 2025 Nov-Dec;15(6):103120. doi: 10.1016/j.jceh.2025.103120. Epub 2025 Jul 29.**

Tuberculosis in Transplant Setting - Implications in Diagnosis, Treatment and

Prevention.

Sahney A(1), Wadhawan M(1).

Author information:

(1)Institute of Digestive & Liver Diseases, BLK Superspeciality Hospital, Delhi,

India.

India is a high endemic country for tuberculosis. The prevalence of tuberculosis

rises in patients undergoing solid organ transplant with a high morbidity and

mortality. Immunosuppressive drugs used after liver transplant have significant

interactions with ATT necessitating changes in approach to treatment of

tuberculosis. Also being a high endemic zone for TB, role of preventive therapy

for latent TB becomes questionable in India. We hereby discuss the diagnostic

strategy, change in drug treatment & role of latent TB in patients undergoing

liver transplant in India.

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training, and similar technologies.

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**74. Open Forum Infect Dis. 2025 Aug 1;12(8):ofaf461. doi: 10.1093/ofid/ofaf461.**

**eCollection 2025 Aug.**

Exploring Mycobacterium riyadhense: Epidemiology, Clinical Presentation, and

Treatment Outcome.

Alsaeed M(1)(2)(3), Alanazi K(1), Alhamdan A(4), Faqihi M(5), Alibrahim A(6),

Alshehri S(7), Shosha D(7), Alraddadi M(1), Alsaeed M(8), Alabdullah M(9), Ahmad

S(2).

Author information:

(1)Medicine Department, Infectious Diseases Division, Prince Sultan Military

Medical City, Ministry of Defence Health Services General Directorate, Riyadh,

Saudi Arabia.

(2)Medicine Department, Dr. Sulaiman Al Habib Medical Group, Riyadh, Saudi

Arabia.

(3)College of Medicine, Alfaisal University, Riyadh, Saudi Arabia.

(4)Department of Adult Infectious Diseases, King Saud Medical City, Riyadh,

Saudi Arabia.

(5)Microbiology Division, Pathology and Laboratory Medicine, Prince Sultan

Military Medical City, Riyadh, Saudi Arabia.

(6)Medicine Department, Infectious Diseases, College of Medicine, Jouf

University, Sakaka, Saudi Arabia.

(7)Medicine Department, Infectious Diseases Unit, Prince Mohammed bin Abdulaziz

Hospital, Riyadh, Saudi Arabia.

(8)Department of Internal Medicine, King Saud Medical City, Riyadh, Saudi

Arabia.

(9)Infectious Diseases Department, Almoosa Specialist Hospital, Al Mubarraz,

Saudi Arabia.

**BACKGROUND:** Mycobacterium riyadhense, an emerging nontuberculous mycobacterium

(NTM), closely resembles Mycobacterium tuberculosis (TB) clinically, often

complicating its diagnosis and management.

**METHODS**: We retrospectively analyzed 8 new cases of M riyadhense infection

diagnosed at Prince Sultan Military Medical City from 2019 to 2024.

Additionally, a systematic review was conducted of 24 previously reported cases

from 2009 to 2025, identified through extensive searches of PubMed and Google

Scholar databases. Data extracted included patient demographics, clinical

features, diagnostic methods, treatments administered, and clinical outcomes.

**RESULTS:** Pulmonary infections were predominant and frequently mistaken for TB,

resulting in diagnostic delays. Extrapulmonary infections included lymphadenitis

and osteomyelitis. A novel association with immune complex glomerulonephritis

was identified. Molecular sequencing was critical in confirming diagnoses due to

limitations in conventional microbiological techniques. Treatment regimens based

on macrolides and fluoroquinolones yielded superior therapeutic outcomes,

exhibiting lower relapse rates and fewer adverse effects compared with

conventional anti-TB therapy. Surgical interventions played a crucial role in

managing complicated or refractory cases.

**CONCLUSIONS**: Enhancing clinical awareness, employing accurate molecular

diagnostic techniques, and adopting targeted antimicrobial therapy are essential

for effective management of M riyadhense infections. Further research is needed

to optimize treatment protocols and improve patient outcomes.

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**75. Clin Case Rep. 2025 Aug 21;13(9):e70807. doi: 10.1002/ccr3.70807. eCollection**

**2025 Sep.**

Pediatric Pott's Disease of the Sacrum: A Case Report.

Mannan A(1)(2), Jahangir Z(1), Owais M(3), Masaad Ahmed MB(4).

Author information:

(1)Pakistan Institute of Medical Sciences Islamabad Pakistan.

(2)Rawalpindi Institute of Cardiology Rawalpindi Pakistan.

(3)Liaquat Universty of Medical & Health Sciences Jamshoro Pakistan.

(4)Faculty of Medicine and Health Sciences University of Gadarif Gadarif Sudan.

Isolated sacral tuberculosis in children is rare and can present without typical

signs of inflammation. Early recognition and initiation of antituberculosis

therapy are crucial to prevent complications such as bone destruction,

deformity, and paraplegia.

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PMID: 40860298

**76. RSC Adv. 2025 Aug 22;15(36):30001-30025. doi: 10.1039/d5ra04238k. eCollection**

**2025 Aug 18.**

Furan-thiazole hydrazone scaffolds as promising antitubercular and antibacterial

agents: synthesis, characterization, bioevaluation and computational analysis.

Sable YR(1)(2), Shinde RA(3), Yasin HKA(4)(5), Ghanwate N(6), Mali SN(7),

Ghotekar SK(8), Gawari DP(2), Sasane DA(2), Adole VA(1).

Author information:

(1)Research Centre in Chemistry, Mahatma Gandhi Vidyamandir's Loknete Vyankatrao

Hiray Arts, Science and Commerce College Panchavati Nashik 422003 Maharashtra

India sabley70@gmail.com vishnuadole86@gmail.com.

(2)Department of Chemistry, Dr Patangrao Kadam Mahavidyalaya Ramanandanagar

(Burli) Palus 416308 Maharashtra India dhaneshgawari8@gmail.com

sasanedinesh25@gmail.com.

(3)Department of Chemistry, Mahatma Gandhi Vidyamandir's Maharaja Sayajirao

Gaikwad Arts, Science and Commerce College Nashik Malegaon 423105 Maharashtra

India rahulshinde843@gmail.com.

(4)Department of Pharmaceutical Sciences, College of Pharmacy and Health

Sciences, Ajman University P. O. Box 346 Ajman United Arab Emirates

h.yasin@ajman.ac.ae.

(5)Center of Medical and Bio-allied Health Sciences Research, Ajman University

P. O. Box 346 Ajman United Arab Emirates.

(6)Department of Microbiology, Sant Gadge Baba Amravati University Amravati

444602 Maharashtra India nirajghanwate@gmail.com.

(7)School of Pharmacy, D. Y. Patil University (Deemed to be University) Navi

Mumbai 400706 Maharashtra India mali.suraj1695@gmail.com.

(8)Centre for Herbal Pharmacology and Environmental Sustainability, Chettinad

Hospital and Research Institute, Chettinad Academy of Research and Education

Kelambakkam 603103 Tamil Nadu India ghotekarsuresh7@gmail.com.

In the search for novel therapeutic agents against tuberculosis and bacterial

infections, a series of furan-thiazole hydrazone derivatives (4a-4n) was

synthesized, characterized and evaluated for antitubercular and antibacterial

properties. The furan-thiazole hydrazone derivatives were characterized using

FT-IR, 1H NMR, 13C{1H} NMR, 19F NMR and HRMS methods. The synthesized compounds

were tested in vitro against Mycobacterium tuberculosis H37Rv, Staphylococcus

aureus, and Escherichia coli. Compounds 4a, 4b and 4c exhibited good

antitubercular activity with MIC values of 3.12 μg mL-1, comparable to the

standard drug pyrazinamide. In antibacterial assays, compound 4g, bearing a

trifluoromethoxy group, demonstrated superior efficacy with inhibition zones of

19 mm (S. aureus) and 17 mm (E. coli). Molecular docking studies further

validated these findings, revealing strong binding affinities of compounds 4a-4c

with M. tuberculosis CYP51 (-10.32 to -10.76 kcal mol-1) and compound 4g with

2,2-dialkylglycine decarboxylase (-9.65 kcal mol-1), suggesting effective

interaction with key active site residues. In silico ADME profiling revealed

favorable drug-likeness and pharmacokinetics for most compounds, while DFT

studies including structure optimization, FMO analysis, reactivity descriptors,

and MEP mapping offered valuable insights into electronic distribution,

reactivity, and potential binding sites of the furan-thiazole hydrazone

derivatives. The results support the candidacy of compounds 4a, 4b and 4c in

antitubercular study, while 4f and 4g as notable antibacterial agents for future

development.

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PMCID: PMC12376867

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**77. J Microbiol Immunol Infect. 2025 Aug 21:S1684-1182(25)00160-4. doi:**

**10.1016/j.jmii.2025.08.012. Online ahead of print.**

Mitigating unfavourable treatment outcomes and acquired rifampicin resistance in

isoniazid-resistant tuberculosis: the role of fluoroquinolone.

Lee PH(1), Liu CH(2), Chan PC(3), Yang YC(1), Chu PW(1), Feng CF(1), Lo HY(1),

Lee CC(1), Chiang CY(4).

Author information:

(1)Centers for Disease Control, Ministry of Health and Welfare, Taiwan.

(2)National Research Institute of Chinese Medicine, Ministry of Health and

Welfare, Taiwan.

(3)Centers for Disease Control, Ministry of Health and Welfare, Taiwan;

Institute of Epidemiology and Preventive Medicine, College of Public Health,

National Taiwan University, Taiwan.

(4)Division of Pulmonary Medicine, Department of Internal Medicine, Wanfang

Hospital, Taipei Medical University, Taiwan; Division of Pulmonary Medicine,

Department of Internal Medicine, School of Medicine, College of Medicine, Taipei

Medical University, Taiwan; International Union Against Tuberculosis and Lung

Disease, Paris, France. Electronic address: cychiang@theunion.org.

**BACKGROUND:** Rifampicin (RMP), ethambutol, and pyrazinamide (PZA) for 6-9 months

were recommended for the management of isoniazid-resistant,

rifampicin-susceptible tuberculosis (Hr-TB), but recommendations on

fluoroquinolones (FQs) were inconsistent. We investigated treatment outcomes and

acquired RMP resistance in Hr-TB compared to isoniazid-susceptible TB (Hs-TB).

**METHODS:** We retrospectively enrolled TB patients notified from 2010 to 2018 in

Taiwan. Logistic regression model was constructed to estimate the odds of

favourable outcomes and acquired RMP resistance. Propensity score matching (PSM)

was conducted to address selection bias.

**RESULTS:** 6115 Hr-TB and 71,184 Hs-TB were included. 25.6 % of Hr-TB and 24.7 %

of Hs-TB had unfavourable treatment outcomes (p = 0.149). 0.9 % of Hr-TB and

0.1 % of Hs-TB had acquired RMP resistance (p < 0.001). In Hr-TB treated with

RMP and PZA throughout regimens and Hs-TB treated with RMP throughout regimens,

unfavourable treatment outcomes (16.1 % vs 13.3 %, p < 0.001), and acquired RMP resistance (1.0 % vs 0.1 %, p < 0.001) was significantly higher in Hr-TB than that in Hs-TB. Among Hr-TB, treatment with FQs were significantly associated

with favourable outcomes (adjOR: 3.18, 95 % CI: 2.45-4.15) and less acquired RMP

resistance (adjOR: 0.16, 95 % CI: 0.05-0.55). FQs remain significantly

associated with favourable outcomes (adjOR 3.44, 95 % CI 2.56-4.63) after PSM.

Of the 747 Hr-TB patients treated with a FQ, one (0.13 %) had acquired FQ

resistance.

**CONCLUSIONS:** RMP and PZA throughout regimens did not completely remove the

influence of isoniazid resistance. The use of FQs was associated with better

treatment outcomes and a lower risk of acquired RMP resistance in Hr-TB but

acquired FQ resistance may occur.

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PMID: 40858395

**78. Int J Surg Case Rep. 2025 Aug 22;135:111855. doi: 10.1016/j.ijscr.2025.111855.**

**Online ahead of print.**

Rectal tuberculosis in a 48-years-old immuno-competent man: A rare case report.

Budha B(1), Dulal AR(2), Bhandari RC(3), Paudel N(4), Pandey S(5).

Author information:

(1)Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University,

Maharajgunj, Nepal. Electronic address: bishalbc265@gmail.com.

(2)North East Medical College, Sylhet, Bangladesh.

(3)Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal.

(4)Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University,

Maharajgunj, Nepal.

(5)Kathmandu University School of Medical Sciences, Dhulikhel, Nepal.

**INTRODUCTION:** Rectal tuberculosis (TB) is one of the rare presentations of

gastrointestinal tuberculosis that often mimics malignancy or inflammatory bowel

disease (IBD), presenting as fistulas, ulcers, and chronic pain. Rectal TB is

very rare in immunocompetent patients. The mainstay of diagnosis is

colonoscopy-guided biopsy. Management rarely requires surgical interventions and

is treated with anti-tubercular therapy responding well.

**CASE PRESENTATION:** A 48-years-old man presented with rectal mass, per-rectal

bleeding, and painful defecation, initially raising concerns of malignancy.

Imaging and colonoscopy revealed ulceration, while histopathology confirmed

granulomatous proctitis of tuberculous origin, which improved significantly with

anti-tubercular therapy.

**DISCUSSION:** Rectal TB can mimic malignancy or IBD demanding early

histopathological confirmation. Timely diagnosis and anti-tubercular therapy

ensures favorable outcomes in affected patients.

**CONCLUSION: T**hough rare, rectal TB should be considered as differential

diagnosis in anorectal lesion, with early histopathological confirmation

essential for effective treatment.

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DOI: 10.1016/j.ijscr.2025.111855

PMID: 40857887

**79. Clin Case Rep. 2025 Aug 20;13(8):e70799. doi: 10.1002/ccr3.70799. eCollection**

**2025 Aug.**

Diagnostic Challenges and Recovery of First Tarsometatarsal Joint Tuberculosis

Extending to Medial Cuneiform and First Metatarsal: A Rare Case Report.

Sweekar D(1), Omkar B(2), Sriram K(2), Sunil B(3), Maya U(4), Shubham P(5).

Author information:

(1)Lalbandi Municipality Hospital Lalbandi Nepal.

(2)Department of Orthopedics Nisarga Hospital and Research Center Kathmandu

Nepal.

(3)Department of Anesthesia Nisarga Hospital and Research Center Kathmandu

Nepal.

(4)Infectious and Communicable Disease Hospital Lekhnath Nepal.

(5)Seti Provincial Hospital Dhangadhi Nepal.

Foot tuberculosis is rare and often diagnosed late due to non-specific symptoms

and lack of typical radiological findings. Early diagnosis and a combination of

anti-tubercular therapy and surgical intervention are crucial for preventing

deformities, ensuring successful recovery without significant long-term

complications.

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**80. Ann Med Surg (Lond). 2025 May 30;87(7):4661-4665. doi:**

**10.1097/MS9.0000000000003450. eCollection 2025 Jul.**

Reactivation of cereberal tuberculosis post-adalimumab therapy for rheumatoid

arthritis: a case report.

Alghazzawi A(1), Al-Frejat Z(1), Ahmad M(1), Barkil F(1), Shammas L(1), Darwish

EA(1).

Author information:

(1)Department of Neurology, Damascus university, Syria, Damascus, Syria.

**INTRODUCTION AND IMPORTANCE:** Patients with rheumatoid arthritis who are treated

with adalimumab have an increased risk of developing latent infections. The

lethal risk of TB encephalitis as a potential manifestation after treatment with

adalimumab should not be overlooked despite its rarity.

**CASE PRESENTATION:** We report a case of a 19-year-old Middle Eastern female who

developed cerebral tuberculosis after receiving adalimumab therapy for

rheumatoid arthritis. The patient was systemically well. Her medical history

included pneumonia, PCOs (polycystic ovary syndrome), and H. pylori gastritis.

Subsequently, she showed signs of anxiety after treatment with adalimumab.

Magnetic resonance imaging (MRI) of the brain revealed a ring-enhancing lesion.

An analysis of cerebrospinal fluid (CSF) failed to detect tuberculosis. The

patient was treated and responded favorably to the tuberculosis standard

four-drug anti-TB regimen (rifampicin, isoniazid, ethambutol, and pyrazinamide)

and continued to show clinical improvement under ongoing treatment.

**CLINICAL DISSCUSION:** Rheumatoid arthritis patients who are treated with DMARDs

are at risk of developing opportunistic infections. While most opportunistic

infections are well understood and have clear symptoms, the rare occurrence of

encephalitis should not be dismissed.

**CONCLUSION:** Although rare, TB encephalitis should be considered in patients

developing neurological symptoms after treatment with Adalimumab.

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**81. Ann Med Surg (Lond). 2025 May 29;87(7):4554-4558. doi:**

**10.1097/MS9.0000000000003337. eCollection 2025 Jul.**

Isolated biliary tuberculosis: a rare case report and diagnostic challenges.

Usman O(1), Basit MA(2), Mazhar M(3), Imtiaz A(4), Sakhawat U(5), Mujahid R(6),

Prakash V(1), Malik MA(3), Khan MW(3).

Author information:

(1)Department of Internal Medicine, Texas Tech University Health Sciences Center

El Paso, The Hospital of Providence-Transmountain, Texas, USA.

(2)Department of Internal Medicine, UHS Wilson Medical Center, New York, USA.

(3)Department of Internal Medicine, Services Institute of Medical Sciences,

Lahore, Pakistan.

(4)Department of Internal Medicine, Vassar Brothers Medical Center, New York,

USA.

(5)Department of Gastroenterology, UHS Wilson Medical Center, New York, USA.

(6)Department of Internal Medicine, Shalamar Medical and Dental College, Lahore,

Pakistan.

**INTRODUCTION AND IMPORTANCE:** Biliary tuberculosis is a rare form of

Mycobacterium tuberculosis infection, accounting for only 0.0-0.1% of all TB

cases in certain settings. Its preoperative diagnosis is difficult due to

nonspecific symptoms and the lack of specific imaging criteria. Often, it mimics

other diseases like cancers and infections, complicating early detection.

**CASE PRESENTATION:** A 51-year-old female with a past medical history of diabetes

mellitus, hypothyroidism, and a biliary stricture following stent placement

presented with nausea, vomiting, loss of appetite, and weight loss for 4 months.

A CT scan revealed an indwelling common bile duct (CBD) stent, mild intrahepatic

biliary ductal dilatation, and pneumobilia. An endoscopic retrograde

cholangiopancreatography (ERCP) procedure was performed with stent exchange.

Initial CBD biopsy showed chronic inflammation, but both biopsy and fine-needle

aspiration (FNA) were negative for malignancy. A subsequent ERCP with additional

biopsies also returned negative results for malignancy, though CBD brushing

tested positive for M. tuberculosis.

**CLINICAL DISCUSSION:** The diagnosis of biliary tuberculosis is challenging due to

its nonspecific presentation. In this case, the positive result for M.

tuberculosis in the CBD brushing led to the diagnosis, even after negative

biopsy and FNA results. Early recognition of hepatobiliary tuberculosis is

crucial as it enables conservative management with stents and anti-tuberculosis

therapy (ATT).

**CONCLUSION:** Biliary tuberculosis, although rare, should be considered in

patients with unexplained biliary symptoms. Timely diagnosis through appropriate

diagnostic procedures can lead to effective treatment with ATT and stenting,

improving patient outcomes, and preventing more invasive treatments.

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**Jul.**

The Burden of Depression and Stigma Among Individuals With Tuberculosis Within

the Integrated Tuberculosis-Mental Health Project: A Multisite Mixed-Methods

Study Protocol.

Murphy-Okpala N(1), Nwafor C(1), Eze C(1), Njoku M(1), Ezeakile O(1), Meka A(1),

Ekeke N(1), Iyama F(1), Egbule D(1), Anyaike C(2), Chijioke-Akaniro O(2), Chukwu

J(2), Kirubi B(3), Creswell J(3), Onu JU(4)(5).

Author information:

(1)Public Health, RedAid Nigeria, Enugu, NGA.

(2)Public Health, Federal Ministry of Health and Social Welfare, Nigeria, Abuja,

NGA.

(3)Public Health, Stop TB Partnership, Abuja, NGA.

(4)Mental Health, Nnamdi Azikiwe University, Nnewi, NGA.

(5)Psychiatry, Federal Neuropsychiatric Hospital, Enugu, NGA.

There is a complex bidirectional relationship between tuberculosis (TB), major

depressive disorder (MDD), and stigma. Despite the significant burden of these

conditions in sub-Saharan Africa, only a few studies have explored their

interplay. The primary aim of this study is to determine the burden of MDD and

the dimensions of stigma among individuals with TB. The secondary aim is to

assess the effectiveness of integrated TB-depression treatment compared to

standard TB treatment. This will be a multistage study utilizing a mixed-methods

design to address the research questions. Stage 1 will use a cross-sectional

design to evaluate the burden of depression and stigma. Depression will be

assessed using the Patient Health Questionnaire-9 (PHQ-9), and stigma will be

measured using Van Rie's TB stigma scales - covering self-stigma, secondary

stigma, community stigma, and stigma among healthcare workers. Stage 2 will

involve a longitudinal follow-up of all eligible participants diagnosed with

both TB and MDD. Participants will receive either integrated TB and MDD

treatment or standard TB treatment, depending on their assigned site. Baseline

assessments will include depressive symptomatology (PHQ-9) and perceived social

support (Oslo Social Support Scale, OSSS). Follow-up assessments will occur at

two weeks, eight weeks, and 24 weeks, using the same instruments. TB-related

outcomes - including treatment continuation, interruption, default, and

mortality - will also be recorded. Stage 3 will use a qualitative approach to

explore the experience and dimensions of stigma from the perspectives of service

users, their family members, and their communities. Weighted prevalence of MDD

will be estimated with 95% CIs. The proportion of participants reporting

experiences of stigma will be described using frequency counts and percentages.

Changes in depressive symptoms over time between the two treatment groups will

be analyzed using mixed ANOVA. Qualitative data will be analyzed thematically.

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**Jul.**

Metastatic Lung Adenocarcinoma Mimicking Miliary Tuberculosis: A Case Report.

Merhi HJ(1), Chamseddine MW(2), Mhaidly AI(3), Al Najjar ZK(4), Raad AR(5)(1).

Author information:

(1)Pulmonary and Critical Care Medicine, Faculty of Medicine, Lebanese

University, Beirut, LBN.

(2)Internal Medicine, Faculty of Medicine, Lebanese University, Beirut, LBN.

(3)General Medicine, Faculty of Medical Sciences, Lebanese University, Beirut,

LBN.

(4)Pathology, Al Rassoul Al-Aazam Hospital, Beirut, LBN.

(5)Pulmonary and Critical Care Medicine, Al Rassoul Al-Aazam Hospital, Beirut,

LBN.

Lung adenocarcinoma (LA) can present with a wide range of morphological patterns

and may mimic disseminated infectious diseases such as miliary tuberculosis

(TB), posing significant diagnostic challenges and potentially delaying

appropriate treatment. We report a case of metastatic pulmonary adenocarcinoma

that was initially misdiagnosed as miliary TB. A 35-year-old nonsmoking male

presented with a progressive dry cough and shortness of breath. Chest imaging

revealed diffuse bilateral micronodules and a pericardial effusion, raising

suspicion for miliary TB. Although acid-fast bacilli smears and a purified

protein derivative test were negative, empiric anti-TB therapy was initiated

based on radiographic findings. Despite treatment, the patient's condition

deteriorated. Further evaluation, including a cervical lymph node biopsy,

unexpectedly revealed metastatic, moderately differentiated adenocarcinoma of

pulmonary origin. A subsequent pericardial biopsy confirmed metastatic

involvement. Anti-TB therapy was discontinued; however, the patient's clinical

status continued to decline. This case highlights the diagnostic challenge of

metastatic LA mimicking miliary TB. In low TB-burden settings, it is essential

to maintain a broad differential diagnosis and to consider alternative

etiologies, such as metastatic malignancies, when confronted with miliary

patterns on chest imaging, particularly in the absence of classic TB risk

factors or poor response to treatment. Tissue biopsy from accessible sites and

immunohistochemistry remain critical for establishing an accurate diagnosis and

guiding appropriate management in such complex presentations. This case

underscores the limitations of relying solely on imaging and reinforces the need

for a thorough diagnostic workup when evaluating diffuse micronodular lung

patterns.

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**Jul.**

Pancreatic Tuberculosis Manifesting as Pancreatic Mass: A Case Report.

Meena AK(1), Agarwal Y(2), Batra N(1), Hajare S(1).

Author information:

(1)Gastroenterology, Jawaharlal Nehru Medical College, Belagavi, IND.

(2)Internal Medicine, Jawaharlal Nehru Medical College, Belagavi, IND.

Tuberculosis (TB) continues to be a major global health burden, particularly in

low- and middle-income countries, where it contributes significantly to

morbidity and mortality. While pulmonary TB is the most common form,

extrapulmonary manifestations, including pancreatic TB, are rare and often pose

diagnostic challenges. Isolated pancreatic TB in immunocompetent individuals is

exceptionally uncommon and is rarely considered in the initial differential

diagnosis of a pancreatic mass. We present the case of a 26-year-old

immunocompetent woman with a six-month history of persistent epigastric pain,

nausea, vomiting, and progressive weight loss. Laboratory investigations

revealed normocytic normochromic anemia and mildly elevated serum bilirubin

levels. Contrast-enhanced computed tomography (CT) of the abdomen demonstrated

pancreatic mass, leading to a provisional diagnosis of pancreatic carcinoma.

However, histopathological examination of the lesion revealed features of an

acute suppurative process. Further analysis of aspirated cystic fluid using the

Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) and Ziehl-Neelsen (ZN)

staining confirmed the presence of Mycobacterium tuberculosis. The patient was

commenced on standard anti-tubercular therapy, which led to marked clinical

improvement. On follow-up, the patient's symptoms had resolved completely, and

repeat imaging demonstrated normalization of pancreatic architecture. This case

highlights the importance of considering pancreatic TB as a diagnosis, even in

immunocompetent individuals, particularly from endemic regions. Limitations of

our study include a short follow-up period and unavailability of endoscopic

ultrasound (EUS) evaluation.

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