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A case for eliminating Widal testing for enteric fever, India

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Enteric fever remains a preventable yet persistent public health challenge in many low- and middle-income countries, particularly in the African and South-East Asia regions.[1] The disease caused by *Salmonella enterica* serovars Typhi and Paratyphi disproportionately affects children, adolescents and young adults, with an estimated global burden of over 14 million cases and nearly 136 000 deaths annually.[1] India carries a substantial proportion of this burden. Hospital-based surveillance in India reports incidence ranging from 12 to 1622 cases per 100 000 child-years among children and 108 to 970 cases per 100 000 person-years among people older than 15 years, highlighting both high burden and substantial uncertainty in measurement.[2] Despite advances in treatment, vaccination and surveillance, progress towards accurate, accessible diagnostics for enteric fever remains limited.[3]

Accurate diagnosis is essential for controlling infectious disease, yet the link between poor diagnostics and antimicrobial resistance remains underappreciated. False-positives lead to

unnecessary antibiotic exposure, while false-negatives delay appropriate treatment and encourage the use of broader-spectrum antibiotics without microbiological confirmation. Both scenarios drive drug resistance. This problem is especially acute for enteric fever in endemic settings, where its clinical presentation overlaps with malaria, dengue, scrub typhus, chikungunya, leptospirosis and other viral fevers. Poor diagnostics affect patient care and weaken surveillance by hindering accurate assessment of disease burden and transmission patterns, compromising vaccine policy and investment decisions. Reliable diagnostics are therefore essential for both patient care and evidence-based public health policy-making. Here, we argue that eliminating inaccurate serological tests, particularly the Widal test, is a needed and achievable intervention for containing the emerging resistance.

In India, where *S. Typhi* already shows widespread antibiotic resistance,[2] continued reliance on inaccurate diagnostics is harmful. Of particular concern is the near-global dissemination of a multidrug-resistant lineage of *S. Typhi* (H58), with inappropriate prescribing driven by inaccurate diagnostics further accelerating the emergence and spread of extensively drug-resistant strains.[4] Blood culture remains the benchmark for diagnosis of enteric fever and provides the added benefit of antimicrobial susceptibility data. However, the sensitivity of blood culture is moderate (50–65%) and is affected by prior antibiotic use,[5] the timing of sample collection and blood volume. Uneven distribution of laboratory infrastructure, availability of trained personnel and quality assurance systems at primary care and district levels further constrain the effectiveness of blood culture.

The Widal test is a widely used diagnostic tool for enteric fever. The test detects antibodies against *S. Typhi* O and H antigens; however, it lacks validated cut-offs for acute disease and shows highly variable sensitivity and specificity in endemic settings.[5] The test's performance is affected by pre-existing antibodies in the population, cross-reactivity with other infections and inability to distinguish acute infection from past exposure.[3] Widal test can be performed as a slide agglutination or a tube agglutination test. The slide test is widely used across India, but well-established thresholds for determining a positive result are lacking. As a result, any visible reaction may be interpreted as a positive result, leading to false-positive diagnoses and unnecessary antibiotic treatment. The tube test, more commonly used in tertiary care centres, can provide more useful information when two blood samples taken at different stages of illness are compared to

detect a rise in antibody levels. However, when performed on a single blood sample, as is often the case in routine practice, the tube test has limited value for diagnosing acute typhoid.

The largest comparative evaluation of typhoid diagnostics to date strengthens support for discontinuing the Widal test.[5] An analysis showed that Widal performs poorly relative to other diagnostics and adds no incremental value when combined with better-performing rapid tests; notably, none of the best-performing diagnostic combinations included Widal.[5] These findings align with a systematic review which concluded that no currently available rapid diagnostic test can reliably replace blood culture.[3] Collectively, the evidence suggests that Widal is both inaccurate and redundant, providing a strong rationale for its phased withdrawal and regulatory restriction. Eliminating Widal would reduce reliance on a poorly performing diagnostic, limit inappropriate antibiotic use resulting from false-positive results and encourage investment in more accurate and reliable typhoid diagnostics.

A retrospective audit of 100 febrile children at a New Delhi tertiary hospital found that, among 54 Widal-positive patients, only five (9.3%) were confirmed by blood culture, while 49 (90.7%) were culture-negative.[6] These findings illustrate the potential consequences of widespread reliance on Widal testing in high-volume settings. In a district hospital outpatient department managing about 1000 febrile patients each month, even a modest false-positive rate could result in many patients being misdiagnosed with typhoid and receiving unnecessary antibiotics, while alternative causes of fever may be missed. Across India, such reliance on Widal testing could therefore contribute to misdiagnosis, inaccurate disease surveillance and avoidable antibiotic use.

Despite longstanding evidence of poor performance and guidance from the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention against its use, Widal testing remains widespread in endemic settings.[7] In Pakistan, the Khyber Pakhtunkhwa province has issued directives to discontinue Widal testing, although enforcement has been inconsistent. Overall, formal regulatory action to restrict Widal testing remains limited, and the test continues to be widely used across many endemic countries, as reliable and affordable diagnostic alternatives remain elusive. India's National Essential Diagnostics List, developed by the Indian Council of Medical Research in alignment with WHO guidance, promotes diagnostics with proven accuracy and does not include Widal test.[8] However, exclusion from the list only limits public-sector procurement; Widal remains legally available through India's Central Drugs Standard Control Organisation licensed channels. Widal is widely used in the private sector,

reflecting limited clinician awareness and gaps in state-level procurement practices. Eliminating Widal testing will require additional regulatory action by the organization, alongside procurement reforms, clinician education and enforcement measures.

India has previously confronted and successfully addressed a similar challenge by banning serological tests for tuberculosis in 2012. More than 1.5 million tuberculosis serological tests, generating a 15 million United States dollars (US$) market, were performed annually before 2012, largely in the private sector. Following WHO's 2011 recommendation against their use, India issued a legally binding notification under the Drugs and Cosmetics Act prohibiting the manufacture, sale, distribution and use of tuberculosis serology kits.[9] However, the ban alone was insufficient. Success required active enforcement, monitoring against substitution with other inappropriate tests, and parallel rollout of a WHO-recommended cartridge-based nucleic acid amplification test through India's national tuberculosis elimination programme. Combined with mandatory notification and the Nikshay surveillance system, this rollout transformed tuberculosis and rifampicin-resistance detection, improved case notification including in the private sector, reduced inappropriate treatment and advanced public–private integration.[10] The tuberculosis experience shows that eliminating an inaccurate diagnostic requires coordinated normative guidance, regulatory prohibition, validated replacement technology and enforcement even in fragmented health systems. Applying similar principles to enteric fever could yield comparable gains in clinical care, antimicrobial resistance containment and surveillance quality, though unlike for tuberculosis, no rapid, accurate test yet exists to immediately replace Widal.

Given the paucity of alternative rapid diagnostic tests, strengthening blood culture capacity at all levels of care is indispensable and has been recommended by the Indian Council of Medical Research. However, such strengthening alone may not suffice, as most febrile patients are managed in peripheral settings with limited access to microbiological testing. What is needed is a diagnostic ecosystem combining culture-based confirmation with validated, affordable point-of-care tools.

Several novel diagnostic approaches are under development. Molecular assays, targeting *Salmonella typhi*-specific genes, offer high analytical sensitivity but face technical challenges related to low bacterial count in blood, cost and infrastructure requirements.[11] Diagnostics based on host response show promise in differentiating enteric fever from other febrile illness, aligning with syndrome-based diagnostic approaches.[11] IgA-based serological assays against antigens such

as hemolysin E have demonstrated improved specificity in endemic populations.[12] Antigen-detection and metabolomic approaches are also being explored for rapid, culture-independent diagnosis suitable for primary care.[11]

However, new innovations must be rigorously validated. Many promising diagnostics fail to translate from research to practice due to inadequate evaluation in real-world settings, lack of affordability or poor integration into health systems. Premature deployment of inadequately validated tests generates unnecessary follow-up testing, inappropriate treatments, hospitalizations and referrals. These wasted resources are especially costly where health budgets are limited. The *Lancet* Commission on Diagnostics frames such diagnostic inefficiencies within a broader diagnostics gap that undermines efficient use of health resources and equity.[13] Policy-makers should recognize the elimination of inaccurate diagnostics for enteric fever as a priority intervention within global antimicrobial resistance and universal health coverage agendas. Six key actions will be helpful in phasing out unreliable tests. First, clear normative guidance from WHO and national authorities explicitly discouraging the use of Widal slide test and similar poorly performing tests. Second, clear guidance about when and how to perform Widal tube test correctly, and wide dissemination of this information. Third, regulatory action to restrict manufacture, distribution and procurement of inaccurate diagnostics. Fourth, investment in laboratory systems, including blood-culture capacity and quality assurance. Fifth, support the development of affordable, high-performance tests tailored to endemic settings, alongside rigorous analytical and field evaluation using standardized, scientifically robust protocols. Finally, clinician and public engagement to shift diagnostic practices.

The fact that no commercially available typhoid rapid diagnostic test exists as an alternative to Widal test exemplifies the hidden toll of diagnostic neglect in global health. While vaccines, antibiotics and surveillance systems have advanced, diagnostics for diseases endemic in low- and middle-income countries have remained stagnant, often to the detriment of patients and health systems. Continued reliance on inaccurate tests such as the Widal test undermines efforts to control enteric fever and contain antimicrobial resistance. Aligning diagnostic practice with scientific evidence is essential for patient safety, antimicrobial stewardship and credible public health data. India's experience highlights both the importance of the problem and the feasibility of solutions. Eliminating inaccurate diagnostics is not a technological challenge but a policy choice.

Competing interests:

None declared.

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