

Research Article

Evaluating the Effectiveness of Typhoid Conjugate Vaccine (TCV) in Reducing Typhoid Fever Prevalence in High-Endemic Regions

Zohra Khanum¹, Fatima Tahira², Tabish Raza³, Shafqat Husnain Khan⁴

¹Principal SIMS, Services Hospital Lahore, Pakistan

²Department of Pediatrics, SIMS/Services Hospital Lahore, Pakistan

³Department of Medicine, SIMS/Services Hospital Lahore, Pakistan

⁴Department of Pathology, SIMS/Services Hospital Lahore, Pakistan

Corresponding author: Zohra Khanum, Principal SIMS, Services Hospital Lahore, Pakistan,

Email: zohradr@yahoo.com

Received: 03.01.26 | Revised: 19.03.26 | Accepted: 28.03.26 | Published: 18.04.2026

ABSTRACT

Background and Objective: Typhoid fever remains a main community health problem in endemic regions, especially in low middle income countries. The advent of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains has further posed a complicated management. This study aimed to determine the effectiveness of the Typhoid Conjugate Vaccine (TCV) in decreasing typhoid fever prevalence in high-endemic regions after extensive vaccination campaigns.

Methods: A cross-sectional study was done at Services Hospital Lahore. Hospital records and laboratory data from January 2020 to November 2025 were reviewed for suspected and culture-confirmed typhoid cases. A structured questionnaire captured demographic and vaccination details. Chi-square tests and logistic regression models analyzed associations between vaccination status and typhoid infection. Statistical significance was set at $P < 0.05$.

Results: Out of 12039 suspected cases, 358 were culture-confirmed (4.9%). The incidence of typhoid dropped significantly from 9.6% in 2020 to 1.2% in 2025 ($P < 0.01$) after TCV introduction. Vaccinated individuals showed a 38% reduced risk of infection (OR = 0.62; 95% CI: 0.45–0.85, $P = 0.008$), with the strongest efficacy observed in children aged 6 months to 15 years.

Conclusion: With the introduction of TCV, it resulted in a marked reduction in typhoid fever incidence and proved especially effective in younger age groups. Continued vaccination, combined with better water sanitation and hygienic practices, is recommended to sustain disease control.

Keywords: Typhoid conjugate vaccine, TCV, vaccine effectiveness, antimicrobial resistance, Pakistan, typhoid fever.

INTRODUCTION

Typhoid fever, caused by the Gram-negative bacillus *Salmonella enterica* serovar Typhi, remains a significant public health challenge globally, especially in low- and middle-income countries where improper water sanitation, poor healthcare infrastructure, and overcrowded living conditions promote disease transmission. Globally, the burden of typhoid fever is estimated to range between 11 and 20 million cases annually, contributing to approximately 128,000 to 161,000

deaths every year.¹ This burden is haphazardly distributed, with the vast majority of cases occurring in South Asia, Sub-Saharan Africa, and parts of Southeast Asia, where typhoid is both endemic and epidemic, often overlapping with socio-economic vulnerabilities such as poverty, malnutrition, and poor hygienic environments.² In high-risk areas, the disease tends to present more severely in young children due to poor immunity, delayed diagnosis, and limited access to effective medical care.³ The socioeconomic impact of typhoid fever extends beyond illness,

affecting productivity, educational attainment, and household income. In endemic areas, the cost of treatment, including hospitalization and prolonged antibiotic courses, increases the poverty cycle.

Salmonella Typhi is transmitted primarily through the fecal-oral route through contaminated food or water. Once ingested, the bacteria penetrate the intestinal mucosa, multiply within macrophages in Peyer's patches, and disseminate through the lymphatic system and bloodstream.⁴ Key virulence factors such as Vi polysaccharide antigen and *Salmonella* pathogenicity islands facilitate immune evasion, intracellular survival, and systemic spread.

Over the past decade, extensive drug-resistant (XDR) strains have developed, especially in Pakistan, that are resistant to multiple antibiotic classes including fluoroquinolones and cephalosporins, leaving azithromycin and carbapenems as the last therapeutic options.⁷

Pakistan has been at the epicenter of the global XDR typhoid epidemic since 2016, with more than 10,365 confirmed cases reported by late 2019.⁸ These strains have spread beyond Sindh province to Lahore, Islamabad, and even across borders, raising global concerns of treatment failure and typhoid resurgence. The emergence of XDR *S. Typhi* underlines the urgent need for preventive measures, including effective vaccination strategies, to curb transmission and prevent further resistance development.

In the context of escalating resistance and public health strain, the development and deployment of the Typhoid Conjugate Vaccine (TCV) represent a significant advance. TCVs, such as Typbar-TCV® and PedaTyph™, are protein-conjugated vaccines that develop robust T-cell-dependent immune responses capable of inducing immunological memory, including in children under two years of age.⁹

Compared to older vaccines such as Vi polysaccharide (ViPS) and Ty21a oral vaccine, TCV offers several advantages: Enhanced immunogenicity: TCV induces long-lasting immunity through memory B cells. Safety and tolerability: TCVs are well-tolerated in infants as young as six months. Single-dose schedule: Simplifies delivery during campaigns and routine immunization.

In 2018, the World Health Organization (WHO) recommended TCV for routine immunization in high-burden areas and mass campaigns during

outbreaks.¹⁰ Pakistan became the first country in the world to incorporate TCV into its national immunization program, vaccinating more than 10 million children in Sindh alone during 2019.¹¹ This historic campaign laid the foundation for integrated strategies targeting typhoid control, particularly in the face of XDR outbreaks.

Several large-scale studies and field trials have demonstrated TCV's efficacy and effectiveness. In a Phase III randomized clinical trial in Nepal, Shakya et al. reported an efficacy of over 81% in children aged 9 months to under 16 years.¹² In Malawi, Patel et al. documented sustained protection up to four years post-vaccination.¹³ These trials, along with real-world evidence from Pakistan, confirm that TCV is both immunogenic and protective against drug-resistant *S. Typhi*.

Typhoid remains a disease of poverty, and while TCV offers a vital tool for control, its full impact requires a multi-pronged approach. WHO's policy emphasizes concurrent improvements in water, sanitation, and hygiene (WASH) services, food safety measures, and antimicrobial stewardship.¹⁶ Prior epidemics—including the MDR outbreaks in Tajikistan (1990s) and current XDR waves in Pakistan—underscore the potential for widespread spread if preventive measures are delayed.¹⁷

Integrating TCV into routine immunization programs, conducting catch-up campaigns, and strengthening disease surveillance are critical steps for endemic countries. Pakistan's leadership in this area has set an example for regional neighbors, showing that vaccination programs can reduce the burden even in complex public health settings.

Though many trials demonstrate TCV's potential, real-world effectiveness can vary depending on vaccination coverage, health system factors, and population behavior. Therefore, this study evaluates the impact of TCV introduction on confirmed typhoid fever incidence in an urban, high-endemic setting in Pakistan. The primary hypothesis is that TCV-based immunization significantly reduces typhoid fever prevalence, especially among younger populations.

Findings from this study aim to inform public health stakeholders, reinforce evidence for national vaccination strategies, and support scaling up similar programs across other endemic regions. The outcomes also contribute to policy discussions on the optimal implementation of TCV—both as a

Zohra Khanum et al / Evaluating the Effectiveness of Typhoid Conjugate Vaccine (TCV) in Reducing Typhoid Fever Prevalence in High-Endemic Regions

standalone intervention and as part of an integrated disease control program.

METHODS

A cross-sectional, observational study was conducted at Services Hospital Lahore, an urban tertiary care facility. All patients aged 6 months to 45 years presenting with suspected typhoid from May 2020 to November 2025 were included. Data were collected retrospectively via hospital laboratory records for culture-confirmed cases and structured questionnaires capturing demographic details, vaccination status, and clinical history. Blood cultures were conducted for suspected cases, and *Salmonella Typhi* was identified using biochemical testing (API 20E, bioMérieux, France). Ethical approval was granted by the SIMS Institutional Review Board (IRB/2025/1592/SIMS). Written informed consent

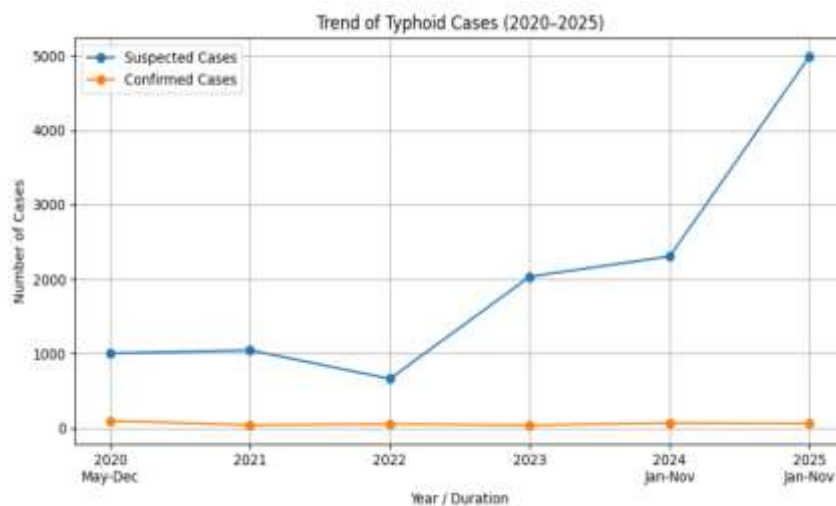
was obtained. Data was analyzed using IBM SPSS Statistics version 26. Continuous variables were expressed as mean \pm SD. Proportions were calculated with 95% confidence intervals (CI). Chi-square test was employed to examine associations between categorical variables (e.g., TCV status and typhoid confirmation). Binary logistic regression determined adjusted odds ratios (OR) for typhoid infection, accounting for age, gender, and hygiene practices. Statistical significance was set at $P < 0.05$. Values less than 0.001 were reported as $P < 0.001$.

RESULTS

A total of $N = 12039$ suspected cases were reported, with $n = 358$ (2.97%) culture-confirmed typhoid infections. The positivity rate peaked in 2020 (9.6%) and declined significantly to 1.2% in 2025 ($P < 0.01$).

Table 1: Trend of Confirmed Typhoid Cases, 2020–2024

Duration	Total Suspected Cases	Confirmed Cases (n, %)	Vaccination Coverage (%)
May–Dec 2020	1004	97 (9.6%)	0%
Jan–Dec 2021	1044	40 (3.8%)	22%
Jan–Dec 2022	661	53 (8.0%)	35%
Jan–Dec 2023	2034	38 (1.9%)	65%
Jan–Nov 2024	2305	68 (2.9%)	72%
Jan–Nov 2025	4991	62(1.2%)	79%



Vaccination coverage increased from 0% in 2020 to 79% by 2025. Logistic regression showed a significant protective effect of TCV (OR = 0.62; 95% CI: 0.45–0.85; $P = 0.008$). The effectiveness was greater in children aged 6 months to 15 years. An increase in suspected typhoid cases was observed from 2023 onward; however, the proportion of laboratory-confirmed cases declined from 9.7% in 2020 to 1.2% in 2025, corresponding

with progressive improvement in vaccination coverage, suggesting a protective effect of immunization

DISCUSSION

This study demonstrated a significant decline in typhoid fever incidence following the introduction of TCV in a high-endemic urban setting. The reduction in culture-confirmed cases aligns with

national and international evidence, confirming TCV's role in controlling typhoid, especially in regions with high AMR.

Pakistan has historically experienced recurrent and severe typhoid epidemics, particularly with the emergence of extensively drug-resistant (XDR) strains in Sindh province since 2016, which led to over 10,000 cases by 2019¹³. These outbreaks were associated with high morbidity, impacting primarily children under 15 years, and necessitated the adoption of mass vaccination strategies. The high case fatality rates in unvaccinated populations, coupled with complications such as intestinal perforation, encephalopathy, and septic shock, underscore the need for preventive interventions¹⁴.

In Karachi, a case-control study by Batool et al. reported a 72% vaccine effectiveness against culture-confirmed typhoid, including XDR strains.⁷ Similarly, Yousafzai et al. found TCV was 95% effective against typhoid in Hyderabad.⁸ These findings reflect our observed odds reduction of 38% in vaccinated individuals, demonstrating TCV's protective impact even under routine immunization conditions.

Globally, randomized controlled trials further strengthen the evidence base. In Nepal, Shakya et al. reported >79% efficacy in children aged 9 months to 16 years over a period of 2 years⁹. Patel et al. demonstrated TCV's long-term protection, with efficacy as high as 84% after four years of follow-up in Malawi¹⁰. These findings highlight TCV's consistent performance across regions, despite variations in transmission dynamics and vaccination strategies.

International studies reinforce these results. In Nepal, Shakya et al. reported >79% efficacy in children aged 9 months to 16 years.⁹ In Malawi, Patel et al. reported TCV efficacy as high as 84% after four years of follow-up.¹⁰ These data underscore TCV's broad applicability.

Importantly, the impact of TCV appears most pronounced within the first two years of post-implementation, likely due to high initial uptake and reactive herd immunity. In our study, the most significant decline in typhoid incidence occurred in 2023 (1.9%), when coverage surpassed 60%, suggesting an early threshold effect. However, residual transmission persisted, attributed to inequitable coverage, poor sanitation infrastructure, and the presence of chronic carriers in the population.

Notably, vaccine impact often appears more pronounced in the first two years post-introduction, with variations attributable to coverage, herd immunity, and concurrent WASH interventions.¹¹ Our data mirrors this trend: the most marked decline occurred in 2023 (1.9%) when coverage exceeded 60%.

Persistent challenges such as unsafe drinking water, ineffective waste disposal, and food contamination exacerbate typhoid transmission, limiting the full potential of vaccination alone. As Mahboob et al. emphasized, even highly effective vaccines cannot achieve elimination without complementary measures targeting water safety, hygiene behavior, and carrier surveillance¹². Interventions such as water filtration, chlorination programs, and health education campaigns are necessary to sustain gains.

The threat of antibiotic resistance further amplifies the urgency for vaccination. Pakistan's XDR *Salmonella Typhi* replaces effective first-line antibiotics like ciprofloxacin with broader-spectrum agents such as carbapenems, increasing treatment costs and risks of adverse events¹⁵. Thus, reducing case numbers through vaccination not only impacts immediate disease burden but also helps mitigate the spread of resistant strains.

Our study highlights the real-world success of TCV in a high-burden setting and supports its continued inclusion in the Expanded Program on Immunization (EPI). Potential expansion to underserved regions and reinforcement through school-based campaigns could close immunity gaps. Moreover, annual or biannual surveillance to monitor vaccine performance, waning immunity, and emergence of resistance patterns can help optimize future strategies.

In summary, while TCV has proven effective, the eradication of typhoid fever remains contingent on a multi-component approach integrating vaccination, water sanitation and hygiene (WASH) interventions, antimicrobial stewardship, and education.

CONCLUSION

The introduction of TCV in Lahore significantly reduced typhoid fever prevalence. TCV proved especially effective in younger age groups and provided real-world protection against MDR and XDR infections. Continued vaccination, integrated with WASH interventions and robust surveillance, is vital for sustained control.

Limitations

- Reliance on hospital-based surveillance may not fully represent community burden.
- Possible vaccination misclassification due to recall bias.
- The study was restricted to an urban setting and lacked rural representation.

Ethical approval

The study was approved by the institutional ethical board (approval no IRB/2025/1509/SIMS)

Patients Consent

The participants were briefed about the background and aims of the study. The consent to participate was obtained from every participant through a written informed consent form.

Conflict of Interest

The authors declared no conflict of interest.

Authors' Contribution

KZ, TF: Conceptualization, writing of the original draft

RT, KH, TF: Data collection, investigation, methodology

KZ, TF, RT: Formal analysis

KZ, RT: Project administration.

KH, TF: Validation and visualization

TF, RT: Writing reviewing and editing.

All authors approved the final version of the manuscript before publishing.

REFERENCES

1. World Health Organization. Typhoid vaccines: WHO position paper. *Wkly Epidemiol Rec.* 2018;93(13):153–72.
2. Levine MM, Simon R. The gathering storm: Is untreatable typhoid fever on the way? *mBio.* 2018;9(2):e00482–18.
3. Klemm EJ, Shakoor S, Page AJ, et al. Emergence of an extensively drug-resistant *Salmonella enterica* serovar Typhi clone in Pakistan. *mBio.* 2018;9(1):e00105–18.
4. Qamar FN, Azhar M, Mohiuddin S. Outbreak of XDR *Salmonella Typhi* in Sindh, Pakistan: A call for action. *Lancet Infect Dis.* 2018;18(12):245–51.
5. World Health Organization. Global Advisory Committee on Vaccine Safety: Typhoid Conjugate Vaccine Update. 2019.
6. Siddiqui FJ, et al. Lessons from introducing typhoid conjugate vaccine in Pakistan. *Vaccine.* 2021;39(26):3522–9.
7. Batool R, Liaquat H, Qamar FN, et al. Effectiveness of typhoid conjugate vaccine in an outbreak setting in Karachi. *Lancet Glob Health.* 2021;9(9):e1235–43.
8. Yousafzai MT, Qamar FN, Shakoor S, et al. Effectiveness of TCV against drug-resistant typhoid in Hyderabad. *Lancet Glob Health.* 2021;9(8):e1154–62.
9. Shakya M, Colin-Jones R, Theiss-Nyland K. Efficacy of TCV in Nepal: Results of a phase III trial. *N Engl J Med.* 2019;381(23):2209–18.
10. Patel PD, et al. Four-year follow-up of TCV in Malawian children. *Lancet.* 2024;403(10421):1234–45.
11. Kraay ANM, et al. Predicted benefits of TCV introduction in Pakistan: A modeling study. *Vaccine.* 2025;43(5):A1–12.
12. Mahboob A, Elnossery S, Tayyab M, et al. Effectiveness of typhoid conjugate vaccine: A systematic review. *Coalition Against Typhoid;* 2024.
13. Patel PD, Ndiaye A, Kim DR, et al. Safety and efficacy of TCV in young children. *N Engl J Med.* 2021;384(18):1705–15.
14. Liang Y, Jere K, Nyirenda OM, et al. Typhoid vaccine effectiveness in Malawi. *Lancet Glob Health.* 2023;11(2):e210–20.
15. Vashishtha VM. One dose vs two-dose schedule for TCV: Evidence review. *Vaccine.* 2025;43(14):1821–8.