



Medical Bulletin

REAL WORLD EVIDENCE ON CLINICAL EFFECTIVENESS AND SAFETY OF CEFIXIME IN MANAGING TYPHOID FEVER IN INDIAN POPULATION

Typhoid fever, also known as enteric fever, is a bacterial infection caused by *Salmonella Typhi*. It is a significant public health concern, affecting approximately 7 million people in South Asia. The contamination of water and food with excretions from individuals carrying *Salmonella Typhi* is a major source of transmitting typhoid fever. Typhoid fever is characterized by a prolonged fever lasting three to four weeks, often presenting with relative bradycardia, gastrointestinal symptoms, involvement of lymphoid tissues, and constitutional symptoms. Certain severe complications may arise including intestinal perforation, hepatitis, gastrointestinal hemorrhage, encephalopathy, myocarditis, acute renal damage, cholecystitis, pneumonia, disseminated intravascular coagulation, and anemia.

Typhoid fever is more prevalent in resource-limited countries compared to their high-income counterparts. Within high income countries, typhoid is largely eradicated due to advancements in sanitation and water treatment. India has a disproportionate burden of typhoid fever, with approximately ten million typhoid fever patients reported in 2021, making India the country with the highest global incidence. Compared to similar developing neighboring countries, India exhibits higher rates of disease, underscoring the urgent need for robust prevention and treatment strategies. To manage typhoid fever, fluoroquinolones have been widely administered to South Asian patients over the past 20 years. However, there has been an increase in the occurrence of resistance to these drugs on a global scale. In India, multidrug-resistant (MDR) strains of *Salmonella Typhi* have been increasingly reported, with a recent study documenting an MDR prevalence of 7% among typhoid patients. Also, they are contraindicated in pediatric patients due to the potential risk of adverse events.

To overcome the challenge of bacterial strains showing antibiotic resistance, it is important to evaluate available and new drugs continuously. Cefixime, is an orally administered third-generation cephalosporin, it is commonly used to treat typhoid fever in both pediatric and adult populations to inhibit *Salmonella Typhi* growth. Cefixime acts by attaching to certain penicillin-binding proteins, disrupting peptidoglycan synthesis and inhibiting cell wall formation, which ultimately results in bacterial cell death. Although cephalosporins were initially considered ineffective against intracellular pathogens due to limited cellular penetration, subsequent clinical studies have validated the efficacy of third-generation agents, such as cefixime, in systemic infections like typhoid fever. Although, fluoroquinolones have better efficacy, cephalosporins are preferred due to their safety properties in children.

The availability of dispersible formulation of cefixime offers several advantages, especially in terms of ease of administration and improved patient compliance. It can be easily dispersed in a small amount of water,

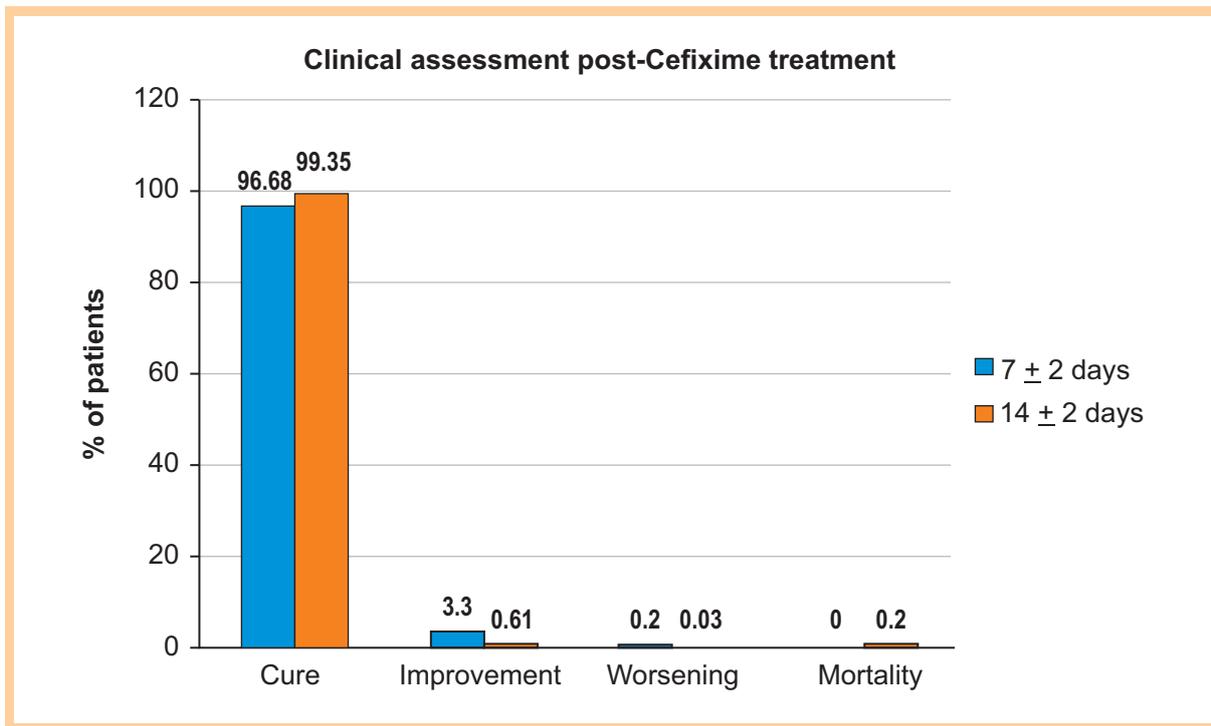
In UTI[†], RTI^{††} & Typhoid

Extacef[®] 200 mg. DT^{*}
Cefixime
Dispersible Tablets



making it ideal for children, elderly patients, or anyone who has difficulty swallowing conventional tablets. Additionally, dispersible tablets often have better palatability, which helps ensure the full dose is taken. By simplifying administration without compromising efficacy, cefixime dispersible tablets support better adherence to antibiotic therapy and more effective treatment outcomes.

In the real-world data, Cefixime, when administered to typhoid fever patients, resulted in clinical cure in over 99% of the patients within two weeks. This demonstrates high activity of cefixime against the causative agent, *S. Typhi*. Serological testing using the WIDAL method showed a progressive decline in positive results throughout the treatment course, further confirming the antimicrobial action of cefixime. Notably, the therapeutic regimen was associated with a low incidence of adverse events. The mortality rate was negligible with only a single fatality reported. Overall, cefixime had a favorable safety profile in the Indian patient population.



The potent activity of cefixime against *Salmonella Typhi* is particularly important, as antibiotic-resistant strains cause treatment failures to existing antibiotics. Presence of transferable MDR plasmids encoding resistance genes against various antibiotics including ampicillin, cotrimoxazole, and chloramphenicol has been long documented in different regions across the globe especially due to TEM-1 β -lactamase production. In contrast, cefixime has demonstrated stability against hydrolysis by several β -lactamases, including TEM-1, allowing it to retain activity against these resistant strains.

In contrast, β -lactam antibiotics, while generally safe for pediatric use, present challenges such as the higher costs associated with parenteral administration and hospitalization, along with the inconvenience compared to oral formulations. Therefore, cefixime has emerged as a feasible, safe, valuable and effective pharmacological & therapeutic option in managing typhoid fever.

Source: Parikh K, et.al; Annals of Medicine and Medical Sciences (AMMS) Volume 04, 2025; Barhate S et.al; IJCRT, Volume 13, Issue 6 June 2025.

In UTI[†], RTI^{††} & Typhoid

Extacef[®] 200 mg. DT^{*}
Cefixime
Dispersible Tablets



[†] UTI: Urinary Tract Infections. ^{††} RTI: Respiratory Tract Infections. ^{*} DT: Dispersible Tablets.

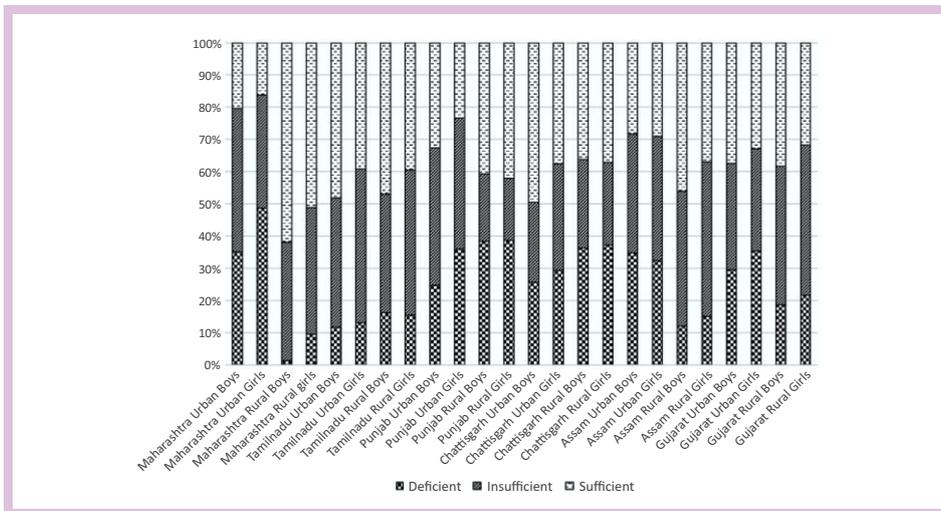
EFFECT OF VITAMIN D SUPPLEMENTATION ON 25-HYDROXY VITAMIN D STATUS IN CHILDREN 12-30 MONTHS OF AGE

Vitamin D (VD) is an essential nutrient in humans, which can be synthesized in the skin after exposure to Ultra violet B (UVB) sunlight rays. It can also be obtained from the intake of foods of vegetable origin (Vitamin D2: Ergocalciferol) or products of animal origin (Vitamin D3: Cholecalciferol). Fruits and vegetables are very low in Vitamin D. Animal products that naturally contain Vitamin D are salmon, eggs, and oils from fish, including cod liver oil. Sun exposure is the main source of circulating Vitamin D and 25-Hydroxyvitamin-D [25(OH)D]. The main functions of Vitamin D include the maintenance of adequate serum levels of calcium and phosphorous for bone health, especially in early childhood. Serum **25-hydroxyvitamin D (25(OH)D)** is the best clinical indicator of vitamin D status. Deficiency in this micronutrient during critical growth periods (such as 12-30 months of age) can impair bone mineralization and increase the risk of rickets, delayed growth, and other health issues like poor modulation of the immune response, and poor regulation of cell growth and proliferation. In addition to its role in bone health, Vitamin D is of importance for many metabolic and physiological processes. Conversely, Vitamin D deficiency has been associated with unfavorable outcomes for human health, among which are autoimmune and allergic diseases such as type 1 diabetes, asthma, respiratory tract infections, chronic diseases such as several types of cancer, and cardiovascular disorders.

It is estimated that Vitamin D deficiency (<50 nmol/L of 25(OH)D) is a global problem affecting approximately one billion people. Although India receives abundant sunlight, vitamin D deficiency remains highly prevalent in Indian children due to factors such as limited outdoor exposure, cultural practices (clothing and sun avoidance), and diets low in vitamin D-rich foods.

Multiple Indian studies indicate a **high burden of hypovitaminosis D** in children and adolescents across various regions:

- National surveys and regional studies show that a significant proportion of Indian children have insufficient or deficient 25(OH)D levels, with estimates ranging broadly but often high (e.g., up to 46-80% in younger age groups and higher with increasing age).
- Factors such as urban residence, female gender, higher BMI, seasonal variation, and limited sunlight exposure are associated with lower 25(OH)D levels.
- Even in the 0-4-year age group, many children exhibit deficient or insufficient vitamin D status when defined using common cut-offs (<50 nmol/L or <20 ng/mL).
- Vitamin D3 (cholecalciferol) is typically more bioavailable and effective at raising serum 25(OH)D than Vitamin D2 (ergocalciferol), as seen in many supplementation studies in children and adults. This is thought to be due to higher affinity and longer half-life in circulation.



For **Prevention & Treatment** of Vitamin D₃ Deficiency

Bluvit-D₃

Cholecalciferol 60,000 IU/ Sachets

Effect of Vitamin D Supplementation on 25(OH)D Levels

A detailed **randomized clinical trial** evaluated the impact of vitamin D supplementation on serum 25(OH)D in children aged **12-30 months**:

Key Findings (Global Trial Evidence)

- Children supplemented with different doses and forms of vitamin D (D2 and D3) for three months experienced statistically significant increases in serum 25(OH)D concentrations compared with controls.
- The mean change in 25(OH)D varied by dosage: supplementation with 400 IU, 800 IU, and 1000 IU resulted in improvements across all vitamin D groups, with 1000 IU showing the greatest increase and the largest reduction in vitamin D deficiency prevalence. No significant adverse effects were reported.
- Although specific large-scale trials on 12-30-month Indian toddlers are limited, extrapolation from broader pediatric supplementation studies (including older Indian school-age children) supports routine vitamin D supplementation in infancy and early childhood improve 25(OH)D status and prevent deficiency-related complications. Indian pediatric guidelines recommend supplementation through infancy and suggest meeting childhood requirements through diet, sunlight, and targeted supplementation in high-risk scenarios. High prevalence and seasonal variability of deficiency suggest that supplementation strategies need to be context-specific, accounting for sunlight exposure patterns, dietary intake, and local deficiency prevalence.
- Current Indian pediatric guidance (e.g., Indian Academy of Pediatrics) recommends:
 - **400 IU/day** of vitamin D during infancy.
 - For children beyond infancy (including toddlers and preschoolers), while routine supplementation is not universally recommended for all healthy children, **adequate intake should come from sunlight and diet**, and supplements (e.g., 600-1000 IU/day) may be advised under physician guidance, especially in confirmed deficiency or risk groups.

Evidence supports the **efficacy of supplements, especially vitamin D3 at appropriate doses**, in raising 25(OH)D levels safely.

Source: Gupta P, et. al; Indian Pediatr. 2022 Feb 15;59(2):142-158. Mario F et. al, Nutrients, 2023, 15(12), 2756; Mustafa A et. al; BMC Pediatr. 2021 Aug 6;21:334. Khadilkar A, et. al; Sci Rep 12, 16790 (2022).

For **Prevention & Treatment** of Vitamin D₃ Deficiency

 **Bluvit-D₃**
Cholecalciferol **800 IU/ml. Drops**



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