

AZITHROMYCIN AND CEFIXIME COMBINATION VERSUS AZITHROMYCIN ALONE FOR THE OUT-PATIENT TREATMENT OF CLINICALLY SUSPECTED OR CONFIRMED UNCOMPLICATED TYPHOID FEVER IN SOUTH ASIA; A RANDOMIZED CONTROLLED TRIAL



**ACT
South Asia**

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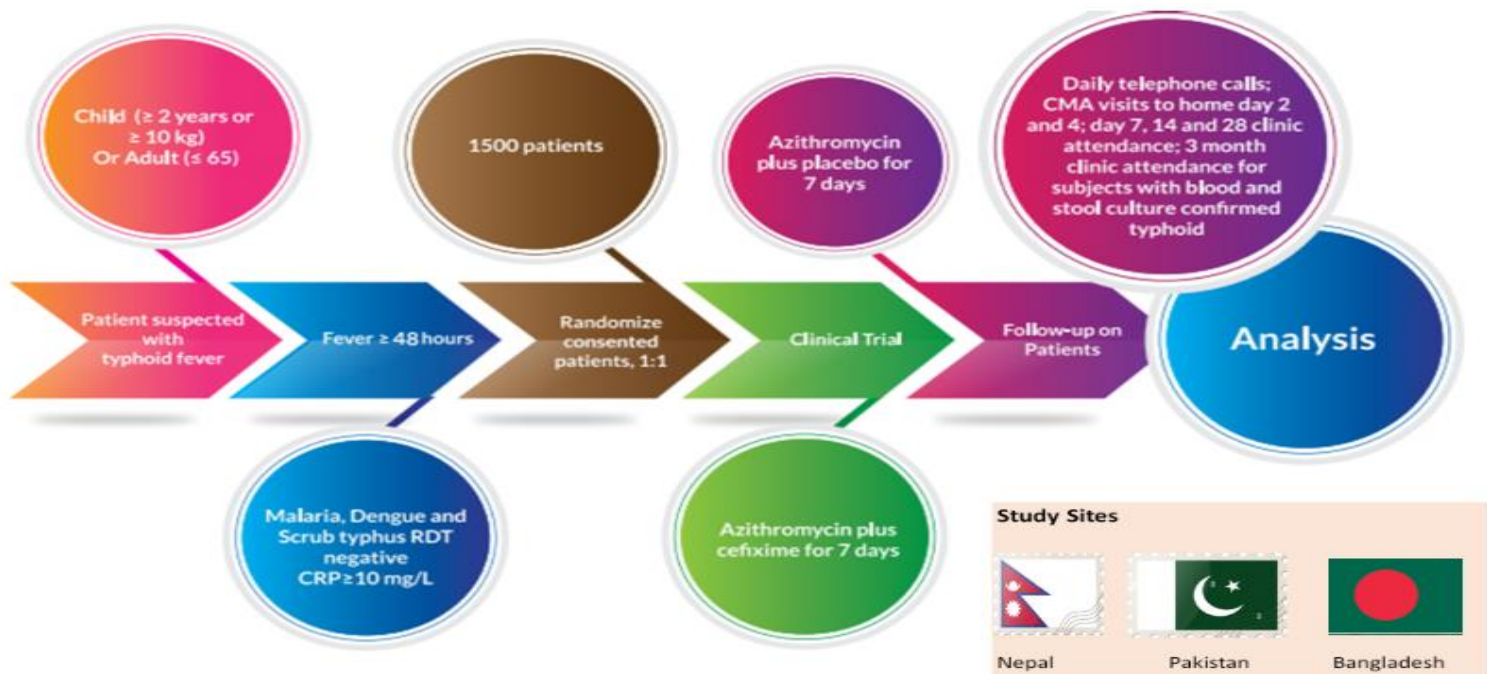
- Enteric fever (typhoid and paratyphoid fever) is a common cause of nonspecific febrile illness in adults and children in low- and middle-income settings
- In South Asia, the incidence can be as high as 500 per 100,000 population.
- Clinicians commonly prescribe a 7 day course of an oral antibiotic, such as azithromycin or cefixime alone, for treatment when this disease is suspected or confirmed.
- Azithromycin is mainly active against intracellular bacteria and cefixime has greater activity against extracellular bacteria in typhoid.
- As activity against both intracellular and extracellular bacteria is thought important in typhoid, we hypothesize that the combination of azithromycin and cefixime will be more effective, with fewer treatment failures, than azithromycin alone

To determine whether treatment with seven days of an azithromycin and cefixime combination is superior to seven days of azithromycin and placebo in preventing treatment failure in patients with clinically suspected or confirmed uncomplicated typhoid fever

Outcome measures: A composite outcome of treatment failure by the 28th day after the initiation of treatment will be defined by either of the following events:

1. Clinical failure: The development of any complication or Syndromic enteric fever relapse within 28 days of initiation of treatment.

2. Microbiological failure: a positive blood-culture for *S. Typhi* or *S. Paratyphi* (on day 7 of treatment) or blood culture-confirmed typhoid fever relapse within 28 days of initiation of treatment.



The study is comparative participant- and observer blind, 1:1 randomized clinical trial, Phase IV, Nepal

Patients with suspected uncomplicated typhoid fever will be randomized

- Arm A: azithromycin 20mg/kg/day oral dose once daily and cefixime 20mg/kg/day oral dose in two divided doses for 7 days,
- Arm B: azithromycin 20mg/kg/day oral dose once daily for 7 days and cefixime-matched placebo for 7 days.

- The study was delayed by COVID-19, but eventually started recruitment in May 2021.
- Patients are being recruited to the study in sites in Nepal, Pakistan, and Bangladesh.
- Till date we have successfully enrolled more than 1200 patients from all study sites. We have recently completed an interim safety and efficacy analysis
- The study aims to recruit >1500 patients from Nepal, Pakistan and Bangladesh by September 2024.

- Azithromycin and cefixime are widely used and safe antimicrobials. But there is uncertainty whether we should use both together, rather than a single drug on its own, for treating typhoid fever.
- This study will determine if using both azithromycin and cefixime together is better than azithromycin alone for treating confirmed or suspected typhoid fever.



STUDY PARTNER

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*Thank
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