

Typhoid versus typhus fever in post-earthquake Nepal



A few months after the 7.8 magnitude earthquake in Nepal on April 25, 2015, and the subsequent strong aftershocks, outbreaks of scrub typhus were reported from various parts of the country, especially from districts affected by the earthquake.¹ These outbreaks were thought to be due to people and rodents (which carry mites with the bacterium *Orientia tsutsugamushi*, the infective microbe in scrub typhus) living in close proximity in temporary shelters after the earthquake. Although typhus in Nepal has been well reported in large studies,^{2,3} the earthquake posed problems in diagnosis and treatment of the outbreaks, primarily because of poor awareness of the disease.

Part of this poor awareness of typhus fever relates to the widespread use of the serological Widal test^{4,5} for typhoid, which often presents with clinical features similar to and indistinguishable from typhus. The Widal test, developed in 1896, is a tube or slide agglutination test that is cheap and simple, but has pitfalls. Cross-reactivity between typhoid, typhus, leptospirosis, malaria, and other prevalent organisms with the Widal test leads to a common misdiagnosis of typhoid fever. This fact is particularly relevant in areas where typhoid is endemic (eg, Nepal) and low background concentrations of typhoid antibodies are present in the normal population.⁴ Additionally, a single acute sample is usually used for testing, but an appropriate cutoff for a positive result can be difficult to establish, because the threshold varies between areas and between times in given areas.

Both typhus and typhoid most commonly present as undifferentiated febrile illness, defined as fever with no localising features,⁶ but have different modes of transmission. Typhoid is transmitted faecal-orally, and typhus is primarily transmitted through insect or mite bites on the skin. *Salmonella typhi* is the main bacterial cause of fever in Nepal and neighbouring countries. Blood culture is the main method of diagnosis for typhoid fever, but because of the paucity of the organism in the blood, the culture growth rates in blood are around 50% at best.⁷ However, in many places in the Indian subcontinent, including Nepal, blood culture facilities are not available, whereas the availability and use of the simpler Widal test is widespread.

The second reason for the poor awareness of typhus fever is that, unlike the availability of the rapid test

for malaria, which is common in the plains of Nepal, point-of-care commercial tests for typhus fever are completely unavailable. Diagnosis of typhus is based on a fourfold increase in serological titre, which is not usually obtained until 3 weeks after testing and can be too late for clinical decision making. Furthermore, cross-reactivity in serological tests occurs, and PCR tests are not often available and are expensive.

As revealed by the post-earthquake outbreaks in Nepal, typhus (scrub typhus in this case) can be deadly because it caused dozens of deaths. Proper diagnosis of this disease is, therefore, essential, especially because the commonly used drug (parenteral ceftriaxone) for undifferentiated febrile illness in Nepal seems to be suboptimal against typhus and common undifferentiated febrile illnesses other than typhoid fever.⁷ Doxycycline is the drug of choice for typhus, but it is not often used in Nepal. Fluoroquinolones have been shown to be effective in typhus;⁸ however, the use of fluoroquinolones for undifferentiated febrile illness (specifically for the common H 58 S typhi clade causing typhoid fever in south Asia) has been challenged.^{9,10} Hence, without rapid diagnostic tests at the start of treatment for undifferentiated febrile illness, establishing whether the patient has typhoid fever, typhus fever, or other causes of fever is difficult. So, to empirically start treatment with fluoroquinolones in a patient with undifferentiated febrile illness in south Asia would not be wise.¹⁰

Although typhoid and typhus might have indistinguishable clinical features, the response to therapy seems to be more prompt for typhus than for typhoid.⁸ Based on these findings at Patan Hospital, once malaria and dengue have been ruled out, we have started to use ceftriaxone and doxycycline in patients with undifferentiated febrile illness of over 38°C for 4 days. If the fever reduces rapidly within 2 days, we assume the patient has typhus fever.

Clearly, improved sanitation and vaccination programmes would be most appropriate, especially for the people living in temporary shelters and districts affected by earthquakes, but this approach requires strong political will. In the meantime, health-care workers need to be able to effectively treat these diseases in an evidence-informed manner.

In conclusion, rapid diagnostic tests to distinguish between typhoid, typhus, and other undifferentiated fevers are urgently needed, particularly after the earthquake in Nepal when 3 million people are still living in shelters. Use of the non-specific Widal test should be discouraged. Finally, after malaria and dengue are ruled out (specifically in the plains in south Nepal), a practical option in the empirical treatment of undifferentiated febrile illness in Nepal would be to start treatment with ceftriaxone and doxycycline.

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I declare no competing interests.

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