

Multidrug Resistant *Salmonella enterica* serovar typhi

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Dear Editor,

Nepal is having a series of enteric fever epidemics over the last decade^{1,2} with changing resistance patterns.³ The first report of multidrug resistant *Salmonella enterica* serovar Typhi in Nepal was published in 1991.⁴ In the following years, with the introduction of fluoroquinolones in the treatment, nalidixic acid-resistant strains associated with reduced susceptibility to fluoroquinolones have been continuously reported from Nepal and trend of resistance is increasing.^{1,5} Subsequently, occasional isolation of highly fluoroquinolone resistant and third generation cephalosporins resistant *S. paratyphi* A and *S. typhi* strains has also been reported from Nepal^{6,7} and other developing countries such as India and Bangladesh.

In July 2008, a *S. typhi* strain was isolated from an enteric fever suspected five year old girl requesting for blood culture at National Public Health Laboratory, Kathmandu, Nepal. Antibiotic susceptibility testing by disc diffusion method showed the isolate was resistant to ciprofloxacin, ofloxacin, tetracycline and cotrimoxazole. Minimum inhibitory concentration (MIC) of the isolate to fluoroquinolone was performed by agar dilution method. The isolate showed complete resistance to nalidixic acid (MIC > 512 µg/mL), ciprofloxacin (MIC, 16 µg/mL), ofloxacin (MIC, 8 µg/mL). Although, high level ciprofloxacin resistant *S. typhi* strain were rare before 2005, the prevalence of such strains in India increased to 6.78% in 2006 from 1.52% in 2005.⁸ In a study carried out in Nepal, all the *S. typhi* and *S. paratyphi*

A isolates were reported as susceptible until 1998 but during 1999 to 2003 ciprofloxacin resistance increased 5% in the *S. typhi* and 13% in *S. paratyphi* A.¹

The full fluoroquinolone resistant strain of *S. typhi* with additional resistance to tetracycline and cotrimoxazole has not been previously characterized from Nepal. Characterization of similar ciprofloxacin resistant strains of *S. typhi* conferring three mutations: two in *gyrA* and one in *parC* and harbouring class 1 integron (*dfrA15/aadA1*) in plasmid that conferred resistance to co-trimoxazole and tetracycline had been reported in 2006 for the first time in India.⁹ The strains of *S. enterica* with multiple resistance mechanisms, have the possibility of becoming resistant to other conventional drugs and third generation cephalosporins by plasmid-borne integron mediated acquisition of resistance gene cassettes.^{9,10} Our *S. typhi* strain having similar multiple resistance pattern with the previously described strain⁹ have the possibility to acquire resistance to cephalosporins and other antibiotics. The prevalence of clone of *Salmonella enterica* resistant to third generation cephalosporins has already been reported⁷ from Nepal. If full fluoroquinolone resistant strain of *S. typhi* as we described acquires resistance to cephalosporins and become predominant, it will limit the existing therapeutic options for enteric fever. An investigation of the extent of full fluoroquinolone resistance problem in *Salmonella* is urgently needed in Nepal.

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