

Changing Pattern of Resistance to Antimicrobials in Patients of Enteric Fever in India in Three Decades: A Systematic Review

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Background: The incidence of typhoid fever in India is rising with pooled estimate of 377 per 100,000 person-years in Delhi and Kolkata, affecting children aged 2-4 years most. Drug resistant typhoid fever has been a major challenge since 1980s. This paper aims to review and synthesize evidence regarding the pattern and trend of antibiotic resistance of *Salmonella typhi* in last three decades in India.

Methods: A systematic search was conducted in Pubmed to include 51 peer-reviewed studies in English language, spanning 36 years till December, 2016. The methodological quality of the studies were assessed using method by Schehner et al, 2013. Three meta-analyses were conducted to determine pooled proportion of resistance of enteric *Salmonella* for each antibiotic in three time periods “1980-1990”, “1991-2000”, “Post 2000”. A meta-analysis was done to determine 5-year period wise pooled proportion of MDR strains and the trend was developed.

Results: A changing pattern of susceptibility from ciprofloxacin and third generation cephalosporins to chloramphenicol, cotrimoxazole, azithromycin is observed between 1980 and 2016. Resistance is highest for nalidixic acid with >90% resistance in last 3 years. 2 studies reported greater proportion of resistance in children compared to adults. Proportion of MDR strains increased from 1980s to 1990s and then again decreased. The pattern of MDR has changed in recent years from ACCoT to plasmid mediated quinolone and 3rd generation cephalosporin resistance. Use of newer antibiotics coincides with decline in MDR for a set of older antibiotics.

Conclusions: Our study provides evidence to inform the stewardship of antimicrobial use as well as ongoing discussion on vaccine introduction under India’s national technical advisory group. While the proposal to increase access to antimicrobials through front-line workers needs to be reformulated by these findings, targeted introduction of conjugate vaccine may also be opted to overcome the challenge of multidrug resistance.