

**Tough times call for rapid techniques: combatting the typhoid superbug**Rohan Kumar Ochani,<sup>1</sup> Ameema Asad,<sup>2</sup> Asim Shaikh,<sup>3</sup> Simran Batra<sup>4</sup>

Madam, typhoid is a highly contagious infection caused by the micro-organism *Salmonella Typhi*. It is transmitted via poor sanitation, over-crowding, and ingestion of contaminated food or water.<sup>1</sup> According to a prospective study conducted by WHO, high incidence of typhoid fever was found in five Asian countries, with Pakistan, India, Indonesia leading and a comparatively lower incidence in China and Vietnam.<sup>2</sup> This geographical dissemination portrays the crucial need to identify fever in its early stages and develop antibiotics to combat the superbug.

The conventional methods routinely used include detection of *Salmonella typhi* in blood, urine, stool, and bone marrow aspirate cultures and antibody detection by the Widal test.<sup>3</sup> However, due to documented cases of false positive results in the past, Widal test is denoted as obsolete. Furthermore, blood culture has 100% specificity, but due to the inaccessibility of obtaining and analyzing cultures in low and middle income countries, the method poses certain limitations. In a clinical setting, a presumptive diagnosis is based solely on clinical presentation, and empirical treatment is initiated before the results of the culture are obtained contrary to the ideal situation of the presence of blood culture result before the first dose of antibiotic is administered. Hence, sensitivity and positive results are decreased in endemic areas due to the unrestrained use of antibiotics and made the grounds for what is known as 'typhoid super-bug'.<sup>4</sup>

Until recently magnetic nanoparticles were coupled with antibodies and greater than 65% *Salmonella typhi* antigen was bound to nanoparticles within 30 minutes. The bacteria were separated from nanoparticles using magnets by heating it at 65°C for 45 minutes. The cells were reheated at 100°C for 5 minutes to break down the covering of bacteria to recover the genetic material. Then the liquid was collected and put through the loop-mediated isothermal amplification

(LAMP) process to increase in availability of genetic material required for identification of the bacteria. This method yielded results with 100% sensitivity, specificity and within 6 hours compared with the sensitivity of blood cultures which is estimated to be around 45-70%. Moreover, isothermal amplification of nucleic acids does not require multiple cycles of rapid heating and cooling which significantly reduces the cost. Hence, isothermal based techniques can be implemented in developing economies.<sup>5,6</sup> It has been reported that superbug strain of salmonella species has also been detected in the aid UK, and has a strong association of travel history from South Asia which regrettably is denoted as a hub of febrile illnesses.<sup>6</sup> This poses an imperative responsibility on Pakistan to explore the strategic use of nanotechnology to reduce the risks of a pandemic in the future. The test can be set-up in Pakistan beginning from Urban cities owing to the accessibility of technology in these areas, then gradually expanding the facilities to a rural setting. Since the majority of cases are due to the causative agent being multi-drug resistant, this technique with its rapid yielding of results will dictate the antimicrobial regimen and avoid unbridled empirical treatment which denotes the basis for microbial resistance. Hence, health authorities in Pakistan should benefit from nanotechnology for diagnosis as set-up by its neighboring country with similar economic burden of diseases.

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