Anti-microbial Resistance surveillance in typhoidal *Salmonella* in Ahmedabad

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Objective

To report on (i) the health care eco-system that produces data on AMR, and (ii) pattern of resistance in typhoidal *Salmonellae* isolates in the city of Ahmedabad in western India.

Introduction

India carries the highest burden of Enteric Fever in the world. This is further aggravated by the high prevalence of antimicrobial resistance (AMR) in typhoidal *Salmonellae*. The strategy to combat resistance has been to combine and cycle anti-microbials based on the regional AMR pattern of the organism. But this requires that resistance patterns and genetic mechanisms are mapped at a regional level and regularly recorded and disseminated by a national surveillance system.

Methods

Through municipality records and internet searches we identified 1696 private and 83 public labs. Our screening of these yielded 4 public medical colleges, 4 private healthcare-institution-attached labs, and 4 corporate labs which were probably performing culture and antibiotic sensitivity testing (AST). Only 2 public medical colleges and 1 corporate lab shared their data with us (Fig 1). There was considerable variation in culturing and sensitivity testing methodology across labs.

Results

Out of 51,260 blood cultures, *Salmonellae* isolates were detected in only 146 (0.28%); 67 (54%) of these were resistant. Multi-drug resistance was absent. The extremely low isolation rates in our three facilities may be indicative of lower referral rates of suspected patients for blood culture or, possibly, lower incidence of *Salmonella* infection in Ahmedabad. Anti-microbial susceptibility testing (AST) was conducted on 124 isolates, of which 67 (54%) were found resistant. Multi- drug resistance was absent, but ciprofloxacin resistance varied widely between the private and public sector labs. The minimal resistance to 3rd generation cephalosporins probably indicates initiation of resistance to this important group of antibiotics in the city's typhoidal salmonella. Notably, isolates from the private sector lab showed complete resistance to azithromycin. Concurrent resistance to more than 1 antibiotic was very high, 88%, amongst the 67 resistant isolates.

Although we were unable to estimate the true size of salmonella positivity against total blood cultures in our city, the difference in proportion of AMR isolates reported in our public and private samples, 30% vs 100%, is important because it may be indicative of high levels of AMR in the private. Notably, isolates from the public sector showed higher resistance to Ciprofloxacin and from private sector showed complete resistance to Azithromycin. The higher Ciprofloxacin resistance in the public sector may be indicative of more usage of the relatively cheaper ciprofloxacin among public hospital clientele. The 100% resistance to azithromycin seen in our private sample is a significant finding, and has also been reported in another recent study from Ahmedabad [1].

Out of approximately 1779 big and small facilities in Ahmedabad, we identified 12 (4 public and 8 private) laboratories which had the ability to report AMR in typhoidal salmonella. 2 public and 4 private refused to share data with us. Based on data shared by 3 medium-sized private facilities, we believe that salmonella isolation and testing in private health-institution-attached laboratories is negligible. Our data collection efforts over one year led to reasonable volume of data from only 2 publicly funded teaching hospitals and 1 private standalone lab.

Although all facilities claimed to follow CLSI guidelines, the total number of antibiotics tested at each facility varied. Minimum inhibitory concentration to assess extent of resistance was not reported by any of the labs. The publicly-funded teaching hospitals

in the city have the largest concentration of microbiologists and the motivation to test for AMR in indoor patients. But they did not consistently test all isolates against all antibiotics in their list. The proportion of private hospitals and laboratories that conduct ASTs in Ahmedabad is relatively small. For individual labs, both private and public, there is no inherent incentive to detect city-level AMR patterns or subsequent molecular level mechanisms of transmission of resistance. This lack of enthusiasm among microbiologists to further process their samples through more specialized lab testing and analysis is an issue in other parts of the world too [2]. Thus patchy performance of AST and incomparability of sensitivity across labs results in poor surveillance [3].

The antibiotic regimen currently recommended by ICMR for treatment of Enteric Fever in the entire country is based on 209 *Salmonella* isolates from only four public institutes [4]. Across India's cities and towns, there are several hundreds of public and private hospitals and laboratories undertaking ASTs, just like the ones in Ahmedabad presented in this study [5]. Unless practitioners are guided by regional data on resistance in endemic organisms, uninformed prescription practices will worsen existing microbial resistance. Drawing these varied facilities, or at least a representative sample of them into a cohesive network is essential for surveillance of antimicrobial resistance in all major bacterial pathogens; particularly so for typhoidal *Salmonella* which are endemic in our part of the world and are primarily exposed to antibiotics consumed by humans since they are obligate human parasites. Only a representative network of labs will provide the contextualized and stratified data necessary for development of the most accurate strategy to formulate regional prescription guidelines. However, this is an enormous challenge in our setting.

Conclusions

High resistance to Ciprofloxacin and Azithromycin in Ahmedabad may be due to increased use of these two antibiotics in the public and private sectors respectively. But they are in need of further molecular characterization.

Clinical microbiological methods lack uniformity and laboratory referral networks are not developed even in large cities of India. Although some useful data is produced by a few individual labs, the crucial exercise of meaningful networking for effective surveillance remains. As we enter an era of internationally linked anti-microbial resistance surveillance systems, the biggest challenge lies in selecting performing laboratories and inducing them to integrate with it.

References

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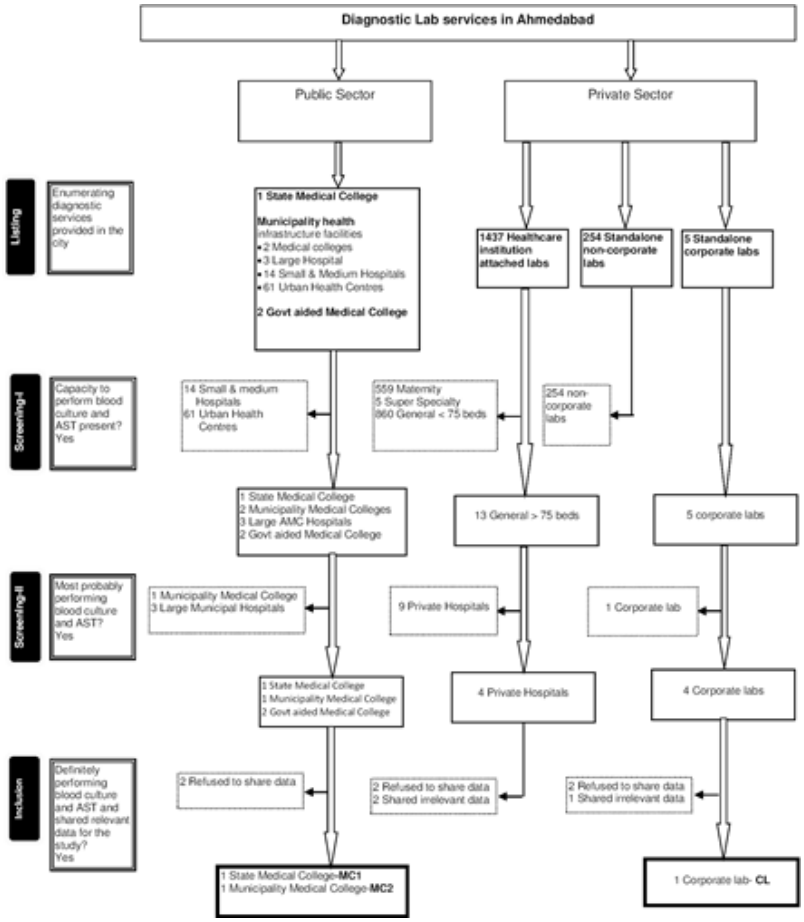

Figure 1.