



MAJOR RESISTANCE PROBLEMS IN INDIA

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Antibiotic resistance is an inevitable consequence of antibiotic misuse the world over. Though the nature of the scourge varies in different parts of the world, the enormity remains the same. Unlike the West where Gram positive infections are the problem, the Indian subcontinent is plagued by resistance in the Gram negative organisms. Drug resistant tuberculosis and malaria also add to our woes.

Though it is acknowledged that antibiotics do not cause mutation in bacteria leading to drug resistance, they are drivers in the selection of resistance. The unregulated use of over-the-counter (OTC) antibiotics, coupled with their use as growth promoters, prophylactic and therapeutic agents in veterinary medicine and agriculture lead to escalation of this problem. Moreover, the rising wave of nosocomial resistance spilling over to community infections is complicating therapeutic interventions as the clear divide of antibiotic sensitivity between nosocomial and community-acquired infections is progressively blurred.

Gram negative organisms account for most of nosocomial infections. Bacteremia is also more commonly due to gram negative infections (over two thirds). *E. coli* and *Klebsiella* are the main culprits.

The challenges associated with antibiotic resistance in India include¹

- Unregulated antibiotic usage
- Poor sanitary standards
- Primitive infection control
- Lack of technical infrastructure to generate data to define the resistance problem

Gram Negative Organisms

The susceptibility patterns of coliforms have significantly changed with a rising ESBL production. The prevalence of ESBL (extended spectrum beta lactamase) *E. coli* and *Klebsiella* are in the region of 65% to 85% in various studies². ESBL production among isolates from patients with nosocomial infection is significantly more than for community-acquired infections (85% vs 53%)³. The commonest source of bacteremia was urinary tract infections (UTI). Colonization of the bowel by ESBL organisms in persons who had not been exposed to antibiotics are over 15%.

Major resistance problems are seen in *Pseudomonas* and *Acinetobacter*. Carbapenem and Ciprofloxacin resistance is 30% to 50% in *pseudomonas* whereas Carbapenem resistance in *Acinetobacter* is 90%^{2, 4}. In general Fluoroquinolone resistance in Gram negative bacteremia is upwards of 70%. Salmonella is the third most common cause of bacteremia after *E. coli* and *Klebsiella*, contributing to over a quarter of cases. The evolution of therapy for *Salmonella typhi* and *paratyphi* reveal a growing resistance to the first line drugs such as Ampicillin, Chloramphenicol and Co-trimoxazole. Subsequently, the MIC (minimum inhibitory concentration) for Fluoroquinolones is showing a rise with restitution of sensitivity to Chloramphenicol⁵. *V. cholera* resistance to Fluoroquinolones has been reported but sensitivity to tetracycline remains.

There have been several risk factors associated with the increased incidence of ESBL producing gram negative bacteria in India. They include

- Increasing use of third and fourth generation Cephalosporins
- Prolonged hospital stay
- Increased severity of illness
- Invasive interventions

Gram Positive Organisms

Penicillin and Fluoroquinolone resistance to *gonococcal* infections is also widespread, warranting treatment of sexually transmitted diseases (STD) with third generation

Cephalosporins or Azithromycin.

Among gram positive cocci, though resistance to Co-trimoxazole for *S. pneumoniae* is rampant, true penicillin resistance is very uncommon (<5%). This is probably related to limited duration of antibiotic exposure due to poverty. There is a rising trend in the MIC of Vancomycin for *Staphylococci*. Though the incidence of MRSA (methicillin resistant *staphylococcus aureus*) varies from 30% to 85%, most hospitals show rates of 30% to 50%. Yet, the creeping MIC of Vancomycin is cause enough for concern. VRSA (Vancomycin resistant *staphylococcus aureus*) have also been identified in India⁶. Daptomyicn MIC is still within the breakpoints for MRSA. A wide variation of VRE (Vancomycin resistant *enterococci*) is seen in Indian hospitals. It is noted to be as high as 40% select tertiary centres, whereas it is very uncommon (< 2%) in most hospitals in India².

Others

Recent trends indicate scrub typhus as an important cause of community fever in several parts of India⁷. Melioidosis is also being increasingly identified as an important agent for sepsis in the community. Fortunately, resistance to conventional agents has not been seen for these infections. Surprisingly, inspite of extensive antibiotic abuse, *Clostridium difficile* has not been identified as a problem pathogen leave alone resistant. It may be due to the higher temperatures seen in most parts of India or due to a protective effect of colonization by multiple resistant coliforms in the gut.

One of the recent developments is the increased detection of nosocomial candida infections in hospitalized patients. Resistance to fluconazole, itraconazole and voriconazole was noted in 7.1%, 9.3% and 8.6% of patients respectively. An increased resistance ($\geq 10\%$) resistance to azoles was noted in *C. albicans*, *C. tropicalis*, and *C. glabrata* strains⁸.

To effectively tackle the major resistance problems in India, legislative measures are required. The interventions should target

- Regulation in the use of Antibiotics
- Increasing awareness about Resistance

- Standardizing effective surveillance
- Strengthening Infection Control to ensure effective isolation, hand hygiene compliance, environmental disinfection and Antimicrobial stewardship

References

1. Raghunath. D Emerging antibiotic resistance in bacteria with special reference to India, *J. Biosci*(4)593-603.
2. Watal C, Goel N, Oberoi GK *et al.* Surveillance of Multidrug Resistant Organisms in a Tertiary Care Hospital in Delhi, India. *J Assoc Physicians India* 2010; 58;Supp32-36
3. Abhilash KPP, Veeraraghavan B, Abraham OC Epidemiology and Outcome of Bacteremia caused by ESBL-producing *E. Coli* and *Klebsiella* spp. In a Tertiary care Teaching hospital in South India. *J Assoc Physicians India* 2010; 58;Supp13-17
4. Shanti M, Sekar U. Multi-drug Resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* infections among Hospitalized Patients: Risk factors and Outcomes; *J Assoc Physicians India* 2009;57:635-45
5. Jog S, Soman R, Singhal T *et al.* Enteric Fever in Mumbai – Clinical Profile, Sensitivity Patterns and Response to Antimicrobials. *J Assoc Physicians India* 2008; 56;237-40
6. Tiwari HK, Sen MR. Emergence of Vancomycin Resistant *Staphylococcus Aureus* (VRSA) from a tertiary care hospital from northern part of India. *BMC Infect Dis* 2006;6:156
7. Vivekanandan M, Mani A, Priya YS *et al.* Outbreak of Scrub Typhus in Pondicherry. *J Assoc Physicians India* 2010; 58;24-28
8. Chakrabarti A *et al.* *Scandinavian Journal of Infectious Disease*; 2009; 41: 275-284