In general, the antimicrobial resistance rates are high in most of bacterial species in China. Pan-drug resistance emerged and has been increasing in some gram-negative bacilli.

1. Staphylococci: Methicillin-resistant *Staphylococcus aureus* (MRSA) and coagulase-negative staphylococci (MRCNS) accounted for 50%-60% and 70%-80%, respectively, in the mainland of China.

2. Enterococci: Less than 5% and 1% of *Enterococcus faecium* and *E. faecalis* are resistant to vancomycin, respectively. Resistance to linezolid occurred.

3. Enterobacteriacae: The produce of ESBL β-lactamases varies in different regions, but the producing rates have been increasing, increased from 18% in 2000 to 60% in 2009 in *Escherichia coli* in Shanghai. A national bacterial resistance surveillance program CHINET showed that ESBLs were detected in 56% and 41% strains of *E. coli* and *Klebsiella pneumoniae*, respectively, in 2009. CTX-M is the major genotype. The resistance rates of *E. coli* to quinolones are very high (approximately 60% to ciprofloxacin) in China. Pan-drug resistant (PDR) *K. pneumoniae* emerged in recent years. The definition of PDR is that a bacterial strain resistant to all antimicrobials but colistin and tigecycline, which are not available currently in China.

4. Non-fermenters: The isolation of non-fermentative gram-negative bacilli such as *Pseudomonas aeruginosa*, *Acinetobacter* spp. and *Stenotrophomonas maltophilia* has been increasing, 30%-40% of gram-negative bacilli clinical isolates are non-fermenters. Non-fermenters are highly resistant to commonly used antimicrobials and notably, the resistance rates of *A. baumannii* to carbapenems have been increasing rapidly in recent years. Approximately 50% of *A. baumannii* strains are resistant to carbapenems currently. The antimicrobial resistance, however, in *P. aeruginosa* keeps relatively stable in recent ten years with the resistance rates less than 25% for ceftazidime, imipenem, cefoperazone/sublactam, amikacin and ciprofloxacin. PDR *A. baumannii* strains have been increased from 2.8% in 2007 to 17% in 2009. NDM-1 β-lactamase gene is present in a few strains of *Acinetobacter* spp..

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 include:

- 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 studies. ESBL production among isolates from patients with nosocomial infection is significantly more than for community-acquired infections (85% vs 53%). 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 Chloramphenicol.

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 India. Daptomycin 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 India.

Others

Recent trends indicate scrub typhus as an important cause of community fever in several parts of India. 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 (>10%) resistance to azoles was noted in C. albicans, C. tropicalis, and C. glabrata strains.

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
Gram Negative Organisms

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Major Resistance Problem in Southeast Asia

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Antimicrobial resistance is prevalent and has been increasing in Southeast Asia (SEA). The major factor associated with high prevalence of antimicrobial resistance in SEA is inappropriate use of antibiotics including an overseuse of antibiotics, and use of low-quality medicines, substandard doses or incomplete course of treatment.

Antimicrobial resistance in SEA is very prevalent in community-acquired infections, healthcare-associated infections and hospital-acquired infections.

For community-acquired infections, the major resistance problems are drug-resistant Streptococcus pneumoniae, drug-resistant enteric pathogens (such as Shigella spp., Campylobacter spp.) and drug-resistant Neisseria gonorrhoeae. Community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) is prevalent in some countries in SEA. Community-acquired extended-spectrum-beta-lactamase (ESBL)-producing gram-negative bacilli have been increasingly detected.

For healthcare associated infections and hospital-acquired infections, the major resistance problems are MRSA, multidrug-resistant Pseudomonas aeruginosa & Acinetobacter baumannii, and ESBL-producing gram-negative bacilli. Carbapenem-resistant gram-negative bacilli have been increasingly isolated. Colistin-resistant Acinetobacter baumannii and vancomycin-resistant enterococci (VRE) is still uncommon in many countries in SEA. Vancomycin-resistant S.aureus has not been observed.

The current situation and the trend of antimicrobial resistance of common causative bacteria causing infections in each country in SEA will be presented and discussed.

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