Can India be the Wing Commander in the Global Fight Against Antimicrobial Resistance?

Abdul Ghafur*

Antimicrobial resistance is a serious global challenge. No continent or country could escape from the wrath and menace of super bugs, only the extend and severity of the problem varies. There could be a return to the pre-antibiotic era where many people suffer or die from untreatable bacterial infections; forcing eminent observers to make superlative pessimistic comments on the future of medicine and civilisation. An overoptimistic section of medical community was extremely critical of this prediction and predictors. The prediction has now transformed into reality; the drama of bugs reclaiming their lost status and the modern medicine watching as a helpless observer with no antibiotics available to treat these infections, however unbelievable and dreadful the scenario may be is being unfolded. Microbes are global citizens: their spread across the earth not being restricted by the national boundaries, color of the human skin or national flags. If we intend to challenge microbes and tackle the situation, we have to pursue the behavior and tactics of bugs, by becoming global citizens and thinking beyond national boundaries.

The controversial Lancet paper on NDM-1 (New Delhi Metallobetalactamase) producing superbugs could generate a discussion on infection control and antibiotic stewardship in India and across the world, at an unprecedented level, probably due to the debate on health tourism and the naming of NDM-1. Not known to most of the public and many medicos; the Lancet paper was not really the first publication on the prevalence of NDM-1 producing bacteria in India. The first major paper on NDM-1 was published in JAPI (Journal of Association of Physicians of India) by a group of researchers from Mumbai Hindu hospital, clearly and unambiguously expressing their concern on the seriousness and potential of this new resistance mechanism. To my luck or bad luck; I received invitation to write an editorial to the article. We used the opportunity to warn Indian physicians on the seriousness and depth of antimicrobial resistance issue in our country. The article and the editorial created widespread discussion among Indian physicians. We could not spread the message beyond the group of our physician friends to the wider medical community or the general public. Then how could the Lancet paper create such uproar? Well; the last paragraph of the article commenting on health tourism triggered an international controversy of unparalleled magnitude; bugs otherwise not considered to have any news value, were transformed into superstars overnight. National and International media reported the controversy with great importance. For the first time, there was a nationwide discussion on antibiotics and antimicrobial resistance in the country. Just like the media in any other country, many good journalists in India used this opportunity to discuss the issue of resistance and raise awareness on the importance of tackling the all important question. At the same time, as usual and expected, some other segments of the media just sensationalized the issue; elaborate debate on health tourism and the naming of NDM-1 ensued and the real, serious issue of antimicrobial resistance was overlooked. Superbug controversy was a typical example of how an important topic can be dealt with in a cinematic way, how the real problems are neglected and irrelevant issues sensationalised and blown out of proportion. The real issue is the menace of antibiotic resistance and the irrelevant issues: undue stress on naming of NDM-1 and the discussion on health tourism. Time to forget the controversy is long overdue. I am sure our country will take the issue on a positive side and use it as an opportunity to tackle resistance and join the global war on resistance.

South East Asia is the major epicenter of Gram negative bacterial drug resistance and Mediterranean countries holding the status of minor epicenter. United states rank first on the Gram positive marathon. Number of bacteria in human body is ten times more than the human cells. Human body possesses 100 trillion cells and the number of bacteria living in human body being ten times the 100 trillion mass. Population of India is 100 times more than the population of Greece, a country with a similar Gram negative bacterial resistance statistics to India. More than half of the world population is living in South East Asia. The bacterial biomass and so the resistance potential of Asian countries, the major epicenter of Gram negative resistance is much more than the minor epicenter of Mediterranean countries.

Extended Spectrum Beta lactamase (ESBL, an enzyme making most of the antibiotics worthless) producing Enterobacteriaceae is the norm rather than exception in most of the major Indian hospitals. Carbapenem group of antibiotics is considered to be the gold standard against severe infection by ESBL producers. Extensive usage of carbapenem group of antibiotics-the most potent antibiotic known to mankind, to tackle ESBL producers, especially in an uncontrolled and unrestricted manner resulted in carbapenem resistance in the form of NDM-1 in India, which is structurally quite different from the KPC type of carbapenem resistance gene prevalent in the west. Patients with severe infection caused by carbapenem resistant bacteria are a common scenario in Indian hospitals and in many countries especially in other south East Asian countries and Mediterranean region. Colistin, a veteran antibiotic used in clinical practice in 70’s, later out of fashion due to availability of more potent and safer antibiotics; was brought back to routine use, to tackle infections caused by carbapenem resistant bugs. Tigecycline, the other antibiotic useful in such infections is unfortunately less useful due to its inability to clear bugs in blood, though useful in tissue infections. Colistin, the last of the available antibiotics, is saving lives of thousands of patients in Indian hospitals and across the globe every day. Colistin resistance, the final stage of the night mare; has become a reality. Medical journals have started reporting scary stories on out breaks of colistin resistant infections; in fact, pan resistant bacterial infections-where no antibiotics are available to treat these bugs; from many countries, including India. Are we facing the end of the world? Definitely NO! Human race and civilizations existed long before Alexander Fleming discovered the first antibiotic, penicillin. World will not face the final day, or may not face armageddon. We will definitely live in a world without antibiotics, return to pre Alexander Fleming era; a civilisation without the basic foundation of modern medicine, without intensive care, not able to perform transplant surgeries; in short, a life not supported by the basics of modern medicine—a science, indispensable to the modern civilized humanity. Dr. Yehuda Carmeli, an eminent Israeli expert predicted a whopping 2.5 million additional annual

*Chennai based Infectious Diseases consultant, Indian co-coordinator of world Alliance against Multidrug Resistant organisms
deaths globally, as a result of lack of antibiotics to treat serious infections. This scenario will unfold in the immediate future and continue for five to seven years until new antibiotics are introduced in to the market.

Pharmaceutical industry stopped investing in antibiotic research due to the lack of profitability. Most of the big pharma companies are based in America, where MRSA infection is more prevalent than Gram negative bacterial infections, a problem more rampant in the developing world. Pharma industry, like any other industry, invests in inventions capable of bringing profit to the company. There is no dearth of antibiotics active against MRSA unlike the dry antibiotic pipeline against Gram negative bugs. Scientific community is not expecting any new antibiotics useful against gram negative bugs in the next five to seven years. Living in a world without antibiotics, considered to be a probability: now becoming a reality. Deaths due to the lack of an effective antibiotic have already started in India and abroad. This unfortunate scenario will reach unbelievable proportions in the next few years. Regions with high resistance rates, like South East Asian and Mediterranean countries will have to face the greatest impact. Scandinavian countries, with the lowest resistance rates may be able to ride through the antibiotic free period with minimum scars.

India has more than 20 thousand hospitals and more than three fourth of a million doctors. No wonder why India, with more than a billion population, with her cultural diversity, socio economic disparity and a large medical community is finding the resistance problem an issue difficult to tackle! Indian hospitals have of varying standards of infection control facilities. Majority of Government district hospitals are struggling to provide basic health care to patients. Implementing antibiotic stewardship and good quality infection control in these hospitals will be a target very difficult to achieve.

Antimicrobial resistance is a global problem. With the exception of few countries in the Scandinavian region, most have reported superbugs. Bacteria producing KPC type carbapenem resistant enzymes originated in America and later spread across the globe. NDM-1 producing bacteria are encountered in Major Indian and South East Asian hospitals on a daily basis. In India antibiotic usage is unregulated and unrestricted. We haven’t opened our eyes, even when a catastrophic scenario is imminent! Presence of superbugs in the country is not a crime, but the denial of resistance and lack of initiation of efforts to tackle this dangerous scenario is indeed an unpardonable sin. Even a miraculous change in the attitude at this stage and initiation of measures at a wartime basis will not prevent the catastrophe. Better late than never! Such measures will definitely reduce the size of the grave yards and number of tombstones by significant extend. Urgent measures should be taken to rationalise the antibiotic usage in the country and to implement better infection control practices in hospitals to reduce the transmission of bad bugs from one patient to the other.

Antibiotic stewardship doesn’t necessarily mean not using antibiotics, but using these medications at the right dose, at the right timing, for the right indication. Using the wrong antibiotic, at an unacceptably low dose, at a very late stage of infection will only irritate the bugs and trigger resistance, indeed with a bad outcome to the patient. Pharma industry should keep this in mind and encourage better and sensible antibiotic usage in the country, rather than blindly believing that an antibiotic policy will only reduce their drug sales.

Health care industry will be adversely affected by the increasing resistance scenario, due to poor outcome of medical treatment, in the absence of back ground support by antibiotics to treat infections. Investors in this industry should have futuristic planning to reduce the impact due to the scenario. Denial of the problem is not a solution. Senior medical advisors must warn politicians on the impact of increasing antimicrobial resistance on the country and advise them on the need of urgent and effective measures to tackle the scenario. For the first time in India a national antibiotic policy was published, albeit as a knee jerk reaction to the NDM controversy. One basic prerequisite to any national policy is participation of all stake holders, especially professional bodies like Indian Medical Association, Association of physicians of India and the Clinical infectious diseases society; who have expert members well versed with writing antibiotic policies. Shortly after the publication, the policy was rejected due to its lack of implementability, by the Honorable health minister himself. Indeed, major recommendations of the policy didn’t suit Indian scenario. How can an antibiotic policy stipulate usage of higher end antibiotics allowed only in tertiary care hospitals; at a time, when plenty of patients with severe infections caused by bad bugs seek medical treatment in ordinary hospitals and nursing homes? We need a new antibiotic policy with proper participation of all stakeholders. Infectious diseases society of America, British Society of Antimicrobial Chemotherapy and similar medical societies in the west have succeeded in convincing their governments on the extreme seriousness of the issue and implementing salvage measures to reduce the time frame and impact of the absence of antibiotics.

All Indian hospitals must have an infection control team, supervising day to day antibiotic usage in the hospital, analysing bacterial resistance trends and advising doctors and hospital management on the effective strategies to tackle infection control issues. Hospitals should report the resistance trends to a body at regional level at predefined intervals and a central body monitoring trends at national level. Each hospital should formulate a restricted list of higher end antibiotics and usage of these drugs should be monitored by the infection control team. Hospital management should realise that increasing antimicrobial resistance will literally weaken the foundation of the hospitals and the health care system. Health care professionals should develop the habit of disinfecting their hands with alcohol hand rub before and after patient contact. Patients infected or colonised with bad bugs should be isolated from other patients and medical staff taking care of these patients must follow proper barrier precautions using aprons and gloves. In western countries patients are encouraged to remind their doctors and nurses to follow these precautions.

Banning over the counter sale of antibiotics is a widely recommended strategy to tackle resistance. This will only work as a long term measure, as implementation will take prolonged period and even if strictly followed, can only curb over usage of first or second line antibiotics. A top to bottom approach, starting with tertiary and secondary care hospitals, as a salvage measure to save whatever antibiotics left, is probably the only way to reduce the duration of the antibiotic free period.

Our country, after centuries of colonial rule and suppression, has come a long way since independence; produced famous scientists who have made significant contributions to the field of science and humanity, possessing a space programme the whole world is jealous of and our political voice well respected by the world. India can lead the world as a commander in the fight against bacterial resistance. First, we have to accept the truth: our home land, like many other countries, is seriously hit by bad bugs seek medical treatment in ordinary hospitals and nursing homes? We need a new antibiotic policy with proper participation of all stakeholders. Infectious diseases society of America, British Society of Antimicrobial Chemotherapy and similar medical societies in the west have succeeded in convincing their governments on the extreme seriousness of the issue and implementing salvage measures to reduce the time frame and impact of the absence of antibiotics.

German philosopher Arthur Schopenhauer aptly said: All truths pass through three stages: first- it is ridiculed, second- it is violently opposed, third- it is accepted as being self evident. While dealing with the truth of antimicrobial resistance; unfortunately, we don’t have time for the evolution of first to the final stage.