Editorial

Drug-Resistant Tuberculosis – Are we Resistant to its Cure?

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There is an increasing concern, and not unsubstantiated, about resistant tuberculosis over the past few months. What has always been a concern for respiratory physicians for the past almost 20 years has emerged as a public health problem more than ever before.

India is home to at least 1.15 million cases of tuberculosis, over 40% of the population is possibly infected by the pathogen, and it is estimated that over 100,000 new cases of multi-drug resistant (MDR) TB occur every year in our country. MDR-TB requires more expensive and less effective medication; add to that more side effects, and you don’t have a pleasant situation at all.

Let us recap a bit. Multi-drug resistant tuberculosis (MDR-TB) cases have been documented over the past many years.1 It was acknowledged then that this disease required a different strategy of treatment and was unlikely to respond to the standard first-line short-course chemotherapy of 6 months duration. With almost no good clinic trials done on this ever-rampant disease, prevalent all over the world, the medical fraternity decided that it probably needed common sense and ‘experience’ to treat this disease rather than solid evidence. This self-imposed decision by a large section of the medical fraternity has led to widespread underuse, misuse and overuse of second-line drugs for tuberculosis. This was not a decision that could have been worse for the patient. If the combination was right for the MDR-TB patient, he stood a chance. If not, he didn’t even stand that chance. Coupled with the right combination of drugs, the doctor had to get more things right. Dose correctly, and for the right duration (whoever knows what that is), and hope the patient doesn’t get unacceptable drug adverse effects. And finally the cost. It hasn’t been uncommon to see the MDR-TB patient buy a month or 2 month’s supply of medication, see some benefit, stop medication, and then decide that he doesn’t need medication any more. “I’m fine. Why should I continue medication, and why should I follow-up with a doctor when I’m well. After all, doctors are meant to be visited when one is sick, not well!” This situation is not uncommon to TB, where stigma and a feeling of well-being early on in the treatment, forces many a patient to default. It happens in diabetes and hypertension as well, though one would imagine much less.

And not to forget the sheer embarrassment of informing family (a prospective spouse can be left uninformed about contagiousness) and friends about the disease. No small wonder that this disease is spiralling in both incidence and prevalence.

The RNTCP programme of 19972 was far better than the NTP of 1962 for sure, but there’s still so much work to be done. India continues to have an annual incidence of more than 2 million TB cases.

Now there’s poly-drug resistant, extremely drug-resistant,3 totally drug resistant4 and so on and so on. When is it going to end? When we run out of drugs or when we run out of money?

news? It is important to realise that the WHO has not recognised the term totally drug resistant as yet, the prime reason being that data on reproducibility and reliability of drug sensitivity tests (DSTs) for second-line drugs are limited and not yet well established. And crucially, correlation of DST results with clinical response to treatment have not been adequately established either. Also, a lot of new drugs we use for refractory MDR-TB have not been tested against these ‘totally resistant’ strains.

Velayati and Udwadia et al highlighted the danger of the strain they cultured at their respective Institutes. I believe the news it made was more important than the strain cultured. As the news went ‘viral’, we were left wondering whether H1N1 was more threatening, or MDR-TB.

The answer is simple.

Why did it make news? – because a common disease in the public domain was being perceived as untreatable, a far cry from reality in the vast majority afflicted with this disease. What did it achieve – the public health and private health practitioners to wake up to the seriousness of issues in mismanagement of TB. I wrote a note7 for the public to make them more aware of the disease, and hopefully (eternally hopeful) that the average Indian patient asks his doctor the right questions.

I believe a lot of India’s health problems stem from illiteracy. Here it’s not the need to read about MDR-TB as much as it is to know your rights as a patient. Doctors in India are often treated as God incarnate, never to be questioned too much, and if questioned, will land up with a possibly shorter consult the next time round, and a possible answer like – “do you or I know better about your disease?... please follow my advice”. Many a hapless patient is faced with this scenario, and then helplessly follows good and (often wrong advice), to then land up with improvement or progression, both of which he doesn’t know how to handle!

So a not too common scenario in asthma for example is that the adult or child feels exceedingly better with inhaled steroid, improves remarkably on lung function, and then just decides that he doesn’t need medication any more. “I’m fine. Why should I continue medication, and why should I follow-up with a doctor when I’m well. After all, doctors are meant to be visited when one is sick, not well!” This situation is not uncommon to TB, where stigma and a feeling of well-being early on in the treatment, forces many a patient to default. It happens in diabetes and hypertension as well, though one would imagine much less. The media has done their job there, and early enough. Chronic respiratory diseases like asthma and COPD (non-communicable) and tuberculosis (communicable) need headlines now – and we hope for the right reasons. Maybe not just for TDR-TB, but for many other reasons!

To come back to MDR-TB - the root cause I believe lies with education of the lay public and with health care providers. The responsibility of educating the lay public must be taken up by the media responsibly, with well-vetted inputs (based on good-quality Grade evidence).5 of physicians. The education

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and up-gradation of physicians cannot be left to the individual physician. Out of the 96 million USD first-line anti-TB drug market in India in 2006, only 24 million USD of drugs were purchased by the public sector, underscoring the importance of the private sector in TB treatment.\(^2\) With private practices in Mumbai often running into late hours (self-imposed largely), and your earning capacity as a private physician being often directly linked to the number of patients you see, it’s no small wonder that physicians may possibly not be updating themselves all the time. Time is money in practice, and unless compulsory updating through enforced CME attendance is implemented, as has recently begun in Maharashtra and Gujarat, it will be a while before the average physician is compelled to update.

We cannot keep blaming patient numbers for a falling standard of healthcare. The larger fault therefore lies with us physicians, and not the ignorant patient. As responsible doctors we need to take the blame in India. Individual excellence is not what we need. We need dedicated teams incentivised to work towards a common goal. As someone said “teamwork is the ability of common people to achieve uncommon results”. No quote would be better placed for the organisation of management of MDR-TB in India.

These teams need excellent leaders too. One team would be insufficient, and the issues vary from a small village in Orissa, to an affluent south Mumbai population to a literate town in Kerala – all could have vastly different issues. A national co-ordinator for a programme needs to factor all this in.

Priorities for such a programme should be:

1. Education about tuberculosis diagnosis to primary care physicians – the back-bone of the health structure of any constituency. If you begin wrong, you will end wrong.
2. Education about tuberculosis treatment to primary care physicians – once you diagnose, you need to treat correctly.
3. Education about follow-up to primary care physicians – just starting a right regimen is not the end of the story. Adherence to full treatment lies equally with the patient. An adherent patient immensely benefits society.
4. Improving the laboratory back-up available to the physician. The current DOT5 plus programme in Mumbai does not incorporate resistance testing to prove XDR-TB. A patient who fails on an MDR regimen (DOTS plus) has to have his sputum sent to one of 3 labs (Delhi/Bangalore/Chennai) for further DSTs. Just imagine the time this would additionally take. Until the results are available, no fresh drugs will be provided. In a disease where time is of the essence in detecting bad disease early, a late change of a failing regimen can have disastrous consequences, both in rendering a patient more ill and possibly more intolerant to new drugs, and on significant occasion rendering a potentially operable (resectional lung surgery) patient, inoperable - due to spread of disease to another lung and/or increasing mycobacterial load in the lungs.
5. A city TB Referral Hospital has recently examined the drug sensitivity data from 100 of its MDR-TB patients. This data (Alpa Dalal, personal communication) suggests that only 16 patients had MDR-TB in its true sense. 59 were pre-XDR, 19 were XDR and 6 were XX-DR – all cultures and DSTs from a National Reference Laboratory in our city. If these patients were to wait for DST results from Chennai (fresh samples), imagine the disastrous consequences.

Using the media well to spread awareness about the disease and the drugs needed. This will armour patients to ask their doctors’ the right questions. I notice Indian patients often fear asking their doctors’ questions. The physician is often put on a pedestal, someone who must never be questioned. The beginning of possible mismanagement, especially if the physician hasn’t updated.

6. Strengthening post-graduate teaching programmes in medicine and respiratory medicine. These post-graduates are our future educators. Poor post-graduate training programmes translate into poorly trained specialist physicians, with obvious consequences.

7. Finally, using responsible pharmaceutical companies to help. Time and again in India we have seen local pharmaceutical industry respond to our health care needs, right from drug pricing to drug availability. There is a notion that the pharmaceutical industry is only here to make profits and often obscenely. This is wrong, and it is not uncommon to see our own Indian companies doing an unparalleled job in improving healthcare in our country, right from improving infrastructure for diagnostics, and to making medicine affordable and accessible to millions of Indians. India has almost all second-line and third-line anti-tubercular medication at some of the lowest prices in the world. Our drugs are cheaper than counterparts available in almost all our neighbouring countries, including Bangladesh, Pakistan, Sri Lanka, the Maldives and Nepal. Let alone more reasonable drug pricing, most of these countries around us don’t even have access to all the drugs. So much for advantage India.

It is not an impossible task to manage this disease in India. It requires trained and committed people, something our country doesn’t lack. If training is an issue, then respiratory physicians should be given the responsibility with the help of the Government, and responsible industry. With diseases like COPD and IPF, training in spirometry and high-resolution CT reading has been significantly looked into by the pharmaceutical industry\(^11\) and responsible organisations\(^11\) in this field already.

We can do much more, and now can only be the time to begin.

References

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