TUBERCULOSIS : THE ARAPEUTIC MUDDLE

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Tuberculosis (TB) is playing hide and seek game with human beings since time immemorial, killing 1 billion people in past two centuries. The World Health Organization (WHO) had declared it as a “Global Emergency” in 1993. Today, one-third of world’s population is infected with tubercle bacilli, as determined by tuberculin skin test. Every year 9 million of those infected develop disease and almost 2 million die out of this curable disease. According to a WHO report published in 1999, burden of TB in India is 36 times more than Leprosy, 13 times more than Malaria and 35 times more than HIV / AIDS, costing India a loss of Rs.13,000 crores directly and indirectly.

DEFINITION

Franciscus Sylvius of Leyden (1614-1672) first employed the term "Tubercles" which means rounded bodies of variable sizes probably seen by him in Autopsy conducted on dead bodies of TB patients. Hence, it was believed in those days that TB patients develop multiple "tubercles" in both lungs. Subsequently, it was known that any dust or biological agent ranging from 2 to 6 microns in length can form "tubercles" in lungs. Hence, here was a clear message to medical faculty to diagnose TB by directly seeing organisms under microscope and not by X-ray image alone which is the most misleading tool, since there are many infections and other agents that lead to formation of "tubercles" and causing similar images on chest X-ray. It is unfortunate to note that still many of us base our diagnosis of TB on X-ray images. Robert Koch on 24th March 1882 made historic announcement of his remarkable discovery of the Causative Organism of TB, the bacillus Mycobacterium tuberculosis (M. tuberculosis), the invisible enemy of mankind. This slightly curved, slender rod, acid fast, immotile, measuring 1 to 4 microns in length and 0.3 to 0.6 micron in breadth does not secrete either endotoxin or Exotoxin. It is covered with a very tough membrane of lipo-protein responsible for its virulence and can easily overcome adverse conditions of non-availability of air and nutrition and can survive as dormant for long periods in the human body. A cavity of about 2 cms diameter in the lung harbours about $10^8$ organisms. The disease spreads through air while TB patients cough out millions of organisms in environment, who hunt susceptible individuals for their growth.

CLINICAL PRESENTATION

The disease may present as acute as well as chronic symptoms. Generally, patient approaches with one or more of the symptoms such as cough for more than three weeks, hemoptysis, chest pain, evening rise in temperature, loss of appetite, lassitude, loss of weight. These symptoms are considered as suggestive of TB, though overlap with many other diseases. Many patients, specially children may present with other manifestations like failure to gain weight and thrive. They are likely to be missed in diagnosis without definite demonstrable evidence. One should note that there are no blood tests available to diagnose TB easily with definite accuracy. It is highly distressing to note that lot of quadriplegia, hemiplegia, paraplegia, headache, convulsive patients are reported to be having TB, depicting the delay in early diagnosis and prompt treatment, since TB affects almost all organs and patients may present with a wide spectrum of clinical symptoms.

Today most of us are infected but not diseased because of our great immune system. Hence this disease is also a disease of Immune deficiency. For instance, persons with HIV infection when cell mediated immunity is compromised, become an easy victim to TB. Tuberculosis kills maximum number of HIV/AIDS patients.

Many studies conducted from time to time have revealed beyond any doubt that TB is an adult disease and maximum number of cases occur mostly at the peak of youth supposed to be in good immunity. It is rather confusing why TB affects mainly youth? Why endogenous reactivation of TB occurs at the youth disproving the theme that TB is a disease due to deficient immunity.

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**DIAGNOSIS**

World Health Organization says "when you use X-ray as the diagnostic tool, you might treat 10 patients for TB, actually only 3 of them would have TB". Shadows on X-rays might be because of lot of other diseases. The only proof is demonstration of *M. tuberculosis* by sputum microscopy alone. World Health Organization in a study conducted at Bombay revealed that only 39% of the qualified doctors advise sputum examination to confirm the diagnosis\(^2\). Studies in Delhi, Karnataka and Tamilnadu revealed that in spite of multiple visits, less than one-third of the patients underwent sputum examination for diagnosis of TB\(^3\&^4\). This confusion of using X-ray and not microscopy as the diagnostic tool exists in spite of more than 100 years of discovery of the causative organism.

One should know that sputum microscopy which is simple, quick and cost effective procedure is not only the diagnostic tool but also a very important tool to monitor the therapy by frequent examinations of sputum to declare patient as "cured", only when sputum examination of patient turns out negative at the end of chemotherapy. There is a need to realise that chest X-ray is sensitive but not specific, but sputum microscopy is close to 100% specific for disease diagnosis\(^5\).

Many doctors still rely on mantoux test to diagnose TB in adults forgetting the fact that in India, by the age of 40 - 45 years, upto 80% are positive to this test, which means person is infected but not diseased. This test many a time remains negative in proven cases of TB. It may also be negative due to other factors namely poor general health, nutrition, immuno-superssion and overwhelming acute illness. However, this skin test is an important aid to diagnose TB in children when considered along with other factors like patient's history, history of contact with a smear positive case, X-ray reports, clinical presentations, sputum microscopy if children are able to produce sputum.

**TREATMENT**

There are only 4 to 5 time-tested, well studied foolproof regimens recommended for treatment of TB with initial intensive phase of 2 to 3 months and continuation phase of 4 to 6 months, with variable combinations of drugs for both the phases. Many of us do not follow this time-tested regimen advised and published by WHO and National TB control programme. Studies conducted among qualified doctors in Bombay and Delhi revealed that almost 80 types of different regimens are used, which are inappropriate, expensive or both\(^38\&^6\). This exists both in private and public health care providers. Today, this inadequate and inappropriate treatment has lead India into worst problem of Multi-Drug Resistant Tuberculosis (MDR-TB) increasing the cost of treatment enormously.

Added to this, the moment the patients feel better, they prematurely stop the treatment without completing the prescribed period of regimen and without getting their sputum examined to declare them as positive or negative. Even doctors do not motivate the patients effectively to complete the treatment and to be declared as 'cured'. Mere completion of treatment is not enough.

In spite of instructions to take all the tablets at a time preferably in the morning, many patients swallow tablets in divided doses. It is also noticed that many doctors themselves advise the patients to take in divided doses not even following guidelines of intensive phase and continuation phase. Many doctors just advise four or five drugs for 9 to 12 months continuously, whereas these drugs are not only costly but also highly toxic. Thus patients and doctors share the responsibility of the worst treatment.

Confusion exists among practicing Obstetricians and Gynaecologists about treatment of TB during pregnancy. As per WHO guidelines -

- Prompt therapy should be instituted to prevent impact on foetus.
- No routine therapeutic MTPs are recommended.
- H R Z E have reasonable safety margin.
- Streptomycin (SM) is contraindicated.
- Pyridoxine: about 10 mg should be supplemented every day along with Anti-TB treatment (ATT).

Another area of confusion in the medical fraternity is about the treatment of extra-pulmonary TB. In both pulmonary and extra pulmonary TB, initial intensive phase of 2 to 3 months remains the same. Only the continuation phase has to be extended in case of following conditions:

**Total period of therapy** (including continuation phase):

- TB meningitis : 9-12 months
- Miliary TB : 8-9 months
- Spinal / Bone TB : 9-12 months
One should note that the main objective of National TB Control Programme is to treat infectious pulmonary TB cases at the earliest to prevent the spread and all the regimens are quite effective. Treatment of TB in HIV positive cases is the same as that in HIV negative TB cases.

In spite of being declared as cured, most of pulmonary TB patients will have old healed cavities throughout their life, making them respiratory cripples and victims for secondary infections. With symptoms almost mimicking symptoms of TB, these patients are mostly in the habit of changing their medical consultants with the habit of hiding their previous illness, thereby receiving repeated fresh-courses of ATT without valid indication. This leads to unnecessary wastage of resources and these drugs many a times can prove lethal to many vital organs in the body. This worst situation is compounded particularly in India by Fake doctors.

Minimum period required to grow the organisms on culture media is 4 to 6 weeks, which is not only costly but not available even in big cities. Further, culture and sensitivity tests to drugs is not a practically convenient tool even in the interest of patient. In treatment failure cases where patient remains sputum positive even after successful completion of treatment of 8 months to 1 year, Physician should employ appropriate treatment regimen immediately, i.e., 2SHRZE + 1EHRZ + 5HRE without doing any culture sensitivity tests. The success rate of this regimen is considerably good. These days, many of us employ the second line drugs costing Rs.2,50,000 for each patient without proper justification.

**PREVENTION OF TUBERCULOSIS**

BCG which is supposed to be the only available vaccine to prevent TB is in the centre of lot of controversy. International policies on the use of BCG vaccine differ from nation to nation. Its efficacy to prevent TB in different trials has been found to range from 0 - 80%. It is said that it can prevent the deadliest type of TB like tubercular meningitis.

In USA, BCG is not recommended routinely. In Eastern Europe, repeat administration is done at school enrolment and school graduation. In Netherlands, it is given only for high risk groups like Hospital health workers, etc. In numerous developing countries including India, BCG is given at birth to at least prevent TB deaths among children due to hematogenous spread. But protection is not absolute and TB does occur in significant proportion of vaccinated individuals. The global challenge for a vaccine that offers complete protection against TB remains at mess.

**Conclusion**

Early detection of "Cases" of TB means detection of patients coughing out *M.tuberculosis* i.e., sputum positive cases. Prompt treatment and curing of these patients is of utmost priority. There is likelihood of prematurely stopping the treatment by the patient for various reasons. Hence supervision to complete the treatment by direct observation through health workers is becoming almost necessary to control this devastating disease.

It is not possible to eradicate TB in the near future because of many man-made reasons and hurdles for his own survival with such a massive load of these deadliest invisible bullets in the environment called *M.tuberculosis* which can prove as lethal weapons against survival of mankind.

**References**


