Tuberculosis - Past, Present and Future

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Tuberculosis (TB) still remains one of the deadliest infectious diseases worldwide. Like some other communicable diseases TB has co-existed with human beings throughout history and has undergone changes in its level of understanding, form, intensity and at times it has come back with new challenges. Human civilization is still striving to eradicate it from the face of the earth by setting this as one of the Millennium Development Goals for the year 2050.

Reality of today is that one third of world population is affected by this disease in spite of the material and technical development and awareness of its etiology, diagnosis and treatment. While significant progress has been made towards the elimination of TB, this disease remains an urgent public health problem in many parts of the world. The most recent 2014 report on tuberculosis by the World Health Organization (WHO) estimated that in 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease, 360,000 of whom were HIV positive.1 A serious concern for TB prevention and control is TB drug resistance and the recent emergence of highly resistant strains which limit the available treatment options for those infected. In 2012, a WHO study revealed the highest ever global rates of multidrug-resistant tuberculosis (MDR-TB) cases of 3.5%2 and these have not changed as yet in the recent report, however higher rates with poor treatment outcomes have been seen in certain regions of the world.1 According to Global Tuberculosis report 2014, 56% of the total 9 million cases fall in the south-east Asia and western pacific region. Pakistan being in this area falls in high TB and high Multidrug-resistant TB (MDR TB) burden countries ranking 5th in the world.1 A high burden country is defined as one where there are 4000 or more new cases of drug-resistant TB per year, or where 10% of new TB cases are drug resistant.

The 2015 Millennium Development Goal for halting and reversing had been set for three targets i.e. incidence, prevalence and mortality and only two out of six WHO regions have achieved all three i.e. the America and western pacific region.1 There was a time in the history, nothing was known about the etiology of this disease and it was by the end of the 19th century, several major breakthroughs gave hope as in 1882, Robert Koch revealed the disease was caused by an infectious agent.3 Further on immunization against tuberculosis was developed and BCG vaccine was first used on humans in 1921 in France.4 It was in 1944 streptomycin, the first antibiotic effective against Mycobacterium tuberculosis was isolated.3 This discovery is generally considered the beginning of the modern era of tuberculosis, although the true revolution began in 1952, with the development of isoniazid, the first oral mycobactericidal drug.5 The advent of rifampin in the 1970s hastened recovery times, and significantly reduced the number of tuberculosis cases. Hopes that the disease could be completely eliminated were dashed in the 1980s with the rise of drug-resistant strains,5 and later on with appearance of HIV epidemic in Africa which brought back the disease in developed countries which had exhibited significant control of the disease by this time. In response to the resurgence of tuberculosis, the World Health Organization issued a declaration of a global health emergency in 1993.6 The factors responsible for the failure to control the spread of the disease were identified, and based on them new strategies were designed and funneled for implementation. West saw the resurgence due to HIV but the underdeveloped world had complex situation and everything seemed secondary to prevailing low socioeconomic conditions and social injustices, in spite of the fact that it was not nineteenth century but twenty first. It is noted that National tuberculosis programs were particularly challenged by multidrug-resistant tuberculosis. Globally, fewer than 2% of the estimated cases of multidrug-resistant disease are reported to the World Health Organization (WHO) and managed according to international guidelines. The vast majority of the remaining cases are probably never properly diagnosed or treated, further propagating the epidemic of multidrug-resistant tuberculosis.

Another point of importance focused was, that for decades there has been little effort to improve techniques for diagnosing tuberculosis,7 consequently tuberculosis tests are...
antiquated and inadequate. These inadequacies are particularly problematic since such tests are generally performed in underfunded and dysfunctional health care systems. The problem is exacerbated by the widespread use of inaccurate and inappropriate diagnostic tools, such as serologic assays, in many countries. Fortunately, in the past few years, several improved tuberculosis tests have received WHO endorsement for widespread use. New automated nucleic acid–amplification test that may allow a relatively unskilled health care worker to diagnose tuberculosis and detect resistance to a key antibiotic within 90 minutes. This test and others that are likely to follow have the potential to revolutionize the diagnosis of tuberculosis. Thus, in the coming years, rapid diagnosis and targeted treatment will hopefully provide the greatest opportunity for stopping the tuberculosis epidemic. In addition to the above noncompliance or abandonment of treatment is identified as the major impediments to effective therapy. To combat these factors, directly observed therapy (DOT) has been widely endorsed. The weakest and controversial element of the DOTS model is reliance upon sputum microscopy, not culture, for diagnosis. In addition to the drawbacks of microscopy described above is its inability to identify drug-resistant strains of TB. Microscopy in developing nations is typically performed on unconcentrated sputum using Ziehl-Neelsen staining. Unfortunately, this system only detects patients with very extensive, typically cavitary, lung disease and roughly one-half of the patients with active pulmonary TB would not be detected by this approach, and these unrecognized patients would continue to spread TB until death or diagnosis intervenes.

In the DOTS model, drug resistance is inferred by failure to respond to treatment, typically after few months of therapy. Hence obvious problems arise from this strategy and foremost is progressive damage to the lungs, even death from uncontrolled disease; that is not all, it fuels the ongoing transmission of microbes that are extremely difficult to treat i.e. cases getting infected from the very start with resistant isolates; and last but not the least is the possibility of “amplifying” drug resistance, e.g. the patient begins therapy with isoniazid and rifampin -resistant disease and, during treatment, acquires resistance to pyrazinamide and/or ethambutol also.

Two types of resistant isolates are posing the problem one is Multidrug-resistant TB (MDR TB) organisms, which are resistant to at least isoniazid and rifampin, the two most potent TB drugs. It is important as these drugs are used to treat as first line therapy for all persons with TB disease. Second is extensively drug resistant TB (XDR TB) organism causing a rare type of MDR TB that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin). Because XDR TB is resistant to the most potent TB drugs, patients are left with treatment options that are much less effective, very costly and more toxic. Hence it has become the need of the day that drug-susceptibility testing be developed for use in all the less prosperous regions of the world. For an effective control of TB especially in countries bearing high burden of the world disease especial measures have to be taken as the problem in these countries is not a standalone but rather multifactorial that is supporting the existence of the disease and also hindering in its eradication.

Diseases are depictive of the social and economic aspect of the society and nations and have strong relation with living conditions at that point in time. We all realize that basic human needs if not fulfilled give rise to problems which are secondary in nature and dependent on the basics. In countries like Pakistan it is not only TB which we are not able to control and still rank fifth in high disease burden countries list, but it is with all other diseases which are eradicable, and polio is another recent example. World is enjoying the fruit of modern development by implementing the control measures but we are caught with a population, majority of which is below the poverty line and until and unless we invest to eradicate the poverty, uplift the socio economic conditions, health, moral values and education of our people and fight against the social inequality, no modern strategy will ever be successful or can be benefited from, and we may continue to lose future Jinnah’s of this strategic nation in spite of living in the twenty first century.

References

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