INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Review Article

TUBERCULOSIS: A PUBLIC HEALTH CHALLENGE: BRIEF OVERVIEW OF LITERATURE

Shazina Saeed [1]*, Shamimul Hasan [2]
Assistant Professor, Amity Institute of Public Health, Amity Univesity, Noida, Uttar Pradesh, India
Assistant Professor, Department of Oral Medicine and Radiology, Faculty of dentistry, Jamia Millia Islamia, New Delhi, India
*Corresponding Author Email: shamim0571@gmail.com

Article Received on: 21/11/15 Revised on: 04/12/15 Approved for publication: 15/12/15

DOI: 10.7897/2230-8407.0711

ABSTRACT

Tubeculosis is a chronic granulomatous infectious disease of worldwide prevalence, mostly affecting the inhabitants of developing countries. The disease is mainly caused by M. tuberculosis, although M. bovis may also be implicated in some cases. The disease has a mention as early as 600 B.C in the Vedas and termed as "King of diseases". In the majority of cases lungs are the target organs, but extrapulmonary cases are also documented. Oral lesions are infrequent, however, a number of cases have shown predominant oral involvement. Diverse diagnostic tools are available to confirm a timely diagnosis, thus, preventing systemic complications. Despite treatment modalities and prevention schemes, tuberculosis still prevails as a threat to public health.
This paper aims to provide a detailed review on the etiopathogenesis, clinical features, diagnosis and treatment of tuberculosis. There is also a special mention on the oral features and the dentist's role in combating the disease.

Keywords: Tuberculosis, granulomatous diseases, Mycobacterium tuberculosis, Oral cavity, diagnostic aids.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious granulomatous disease caused mainly by Mycobacterium tuberculosis, an acid-fast bacillus that is transmitted primarily through the respiratory route through inhalation of infected airborne droplets containing the bacillus, M. tuberculosis. Less commonly, TB is caused by exposure to Mycobacterium bovis through ingestion of unpasteurized, infected cow's milk or other atypical mycobacteria.[1]
Though India is the second-most populous country in the world, one fourth of the global incident TB cases occurs in India annually. At 2012, out of the estimated global annual incidence of 8.6 million TB cases, 2.3 million were estimated to have occurred in India.[2]
Tuberculosis remains the leading cause of death worldwide from a single infectious organism. Approximately 32% of the world's population is infected with tuberculosis and an estimated 2 million people die annually from this treatable disease.[3]
Tuberculosis have been recognized for many years as an occupational risk for health care workers, especially the dentists. The possibility that dentists may contract an infection from this contact with living tubercle bacilli in the mouths of patients who have oral tuberculosis or pulmonary tuberculosis is a problem of great clinical significance.[4]

DISCUSSION

Tuberculosis is broadly divided as pulmonary and extra-pulmonary, based on the target organ involvement. Pulmonary tuberculosis accounts for the vast majority of cases, and extra-pulmonary involvement in tuberculosis is uncommon, contributing for approximately 10% to 15% of the cases.[5] TB primarily involves the lungs, although, intestine, meninges, bones, joints, lymph glands, skin and other tissues of the body may also show involvement.[6]
General signs and symptoms include chronic cough with blood tinged sputum, fever, chills, night sweats, loss of appetite, weight loss, fatigue and sometimes finger clubbing.[7]
Oral lesions are usually secondary to a pulmonary disease, and rarely have a primary focus. The microorganisms are carried in the sputum and a breach in the surface facilitates their entry to the mucosal tissues. It is also possible that they are carried through the hematogenous route, deposited in the submucosa, and subsequently to proliferate and ulcerate the overlying mucosa.[8] Gingiva and mucobuccal folds are the common sites of involvement in primary oral tuberculous lesions, although, an inflammatory focus adjacent to teeth or tooth extraction sites has also been reported. In addition, primary lesions are often associated with enlarged cervical lymph nodes. The secondary form is more frequent in middle-aged and older persons and involves mainly the tongue and hard palate.[8]
Tuberculous ulcer, Tuberculous gingivitis, Tuberculous lymphadenitis, Tuberculoma, Tuberculous osteomyelitis, Tuberculous sialadenitis, and Tuberculous involvement of the Temporomandibular jaw are the major forms in which tuberculosis may manifest in the orofacial region.[6,9]
Early and accurate diagnosis of this dreaded public health hazard is mandatory to combat tuberculosis. Interdisciplinary involvement of varied specialists of medical and dental faculty enhances the possibility of an early and effective diagnosis of this condition.
A wide range of conventional and advanced diagnostic aids are available these days, and proper utilization of these diagnostic aids and interpretation by a skilled personnel makes an early and effective diagnosis. Hence, the treatment protocol is established, thereby delaying the complications.

Diagnostic Techniques [10]

Diagnostic Tool	Method /Inference	Advantages	Limitations
TUBERCULIN SKIN TEST [TST]			
Heaf test	Multiple gun injects Multiple samples of testing serum over the flexor surface of the forearm in a circular pattern of six. Read in 3-7 days. Graded into 4 types.	Easier to interpret, with less inter observer variability. Less training required to administer and to read the test.	Multi puncture method 6 pricks-6 injections.
Mantoux test	5 tuberculin units injected intradermally and read 48-72 hours later. Positive when induration of 5-15 mm is seen Areas of calcifications, cavities or radiolucency (darkened areas) Infiltrates or consolidation.	Used as a screening tool. Helpful in diagnosis of active TB. More precise than radiographs Easy to perform.	Not recommended in; Infants less than 12 weeks Post montoux reaction ≥ 15 mm Previous TB disease.
RADIOGRAPHS			Exposure to X rays. Poor sensitivity. Cannot distinguish between active TB and healed TB in case of scar formation.
STAINING			
Ziehl- Nelson staining	Acid fast bacilli are seen as bright red rods against blue, green or yellow background.	Simple method, economical non invasive.	Less than 10^4 Mycobacteria / ml gives negative results.
Auramine fluorescence	Visualizes acid-fast bacilli as bright rods against dark background using fluorescent microscope.	Contrast bacilli can be readily seen under the high dry objective. More sensitive Less tiring Quick results for large number of slides.	Similar appearance may be seen with saprophytic mycobacteria. Requires expensive equipment Used as a screening tool, not for final diagnosis
Enzyme linked immunosorbent assays (ELISA)	Detects the presence of IgG and IgM antibodies when cultured with highly purified A 60 antigen extracted from mycobacteria.	More sensitive than staining Simple method Faster results	A60 antigen is common antigen to various species of mycobacteria leprae, tuberculosis and bovine.
Interferon Release Assays (IGRAs)			
Quanti FERON TB Gold	Amount of Interferon gamma (IFN-Y) in response to contact with the TB antigens is measured.	Results within 24 hours Does not boost responses measured by subsequent tests, which can happen with tuberculin skin tests (TST)	Blood samples must be processed within 12 hours after collection while WBCs is still viable.
T-SPOT. TB	A number of peripheral blood mononuclear cells used in the assay are quantified and enumerates individual T cells producing IFN-Y after antigenic stimulation, thus gives an overall measurement of antigen load on the immune system.	Not affected by prior BCG vaccination Faster results (within 24 hours) Allows the physicians to treat and control the disease much better	More data on the effectiveness of these tests in HIV-infected patients, young children, and other vulnerable groups are needed.
CULTURE	When grown on LJ media, M. Tuberculosis appears as brown granular colonies (buff, rough and tough)	Less expensive than BACTEC Less chances of contamination	To proceed within 6t hours of veni puncture.
a. Lowenstein – Jensen media (LJ media)	Detects the presence of oxygen in fluorescence by scanning it after every hour. Positive sample may contain 10^5 – 10^6 CFU/ml.	Early detection Differentiates M. Tuberculosis from other Mycobacterium species. More sensitive than conventional LJ media	Takes 4-6 weeks to get visual colonies on media. No differentiation between M. Tuberculosis and other Mycobacterium species.

b. BACTEC			Expensive More medical technologist required. More risk of contamination
POLYMERIZED CHAIN REACTION (PCR)	Helps in the detection of infectious agents and the discrimination of non-pathogenic from pathogenic strains by virtue of specific genes.	Very small size of DNA is amplified easily High sensitivity of PCR permits virus detection soon after infection and even before the onset of disease.	Localization within tissues is not possible. Staging of mycobacterial disease is not possible.

TREATMENT AND VACCINES

The course of TB treatment depends on the stage of infection, be it active or latent and also on the individual's risk. If a person has recently come into contact with an infected individual and a TST is negative, LTBI treatment can be started and continued if the TST result is positive after a 12-week window; HIV patients usually continue treatment, though the TST result might be negative. [11] TB is usually treated using multiple drugs together in a mixture, with an intensive 2-month initial phase followed by a 4 to 6 -month continuation phase.[12]

Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PZA), and either Ethambutol (EMB) or Streptomycin (SM) are usually the drugs of choice for the treatment of TB.[12,13] The cocktail mixture of drugs can be changed depending on the stage of infection. A drug regimen chart created by the Centers for Disease Control and Prevention (CDC) outlines the intervals and doses for drug treatment during the specific phases.[13] For example, if the MTB isolate is fully susceptible, either EMB or SM are discontinued, and PZA can be discontinued after two months of treatment. INH and RIF are continued for four months. Treatment can last from six to nine months,[11,13] or even up to twenty months.[11]

Although the Bacillus Calmette-Guérin vaccine (BCG) protects young children against serious forms of TB by mimicking the natural immune response to infection, protection against pulmonary TB is variable.[14] Even after being used for several years, its efficacy is mostly limited to provide immunity to adults with pulmonary TB in highly endemic areas. Efforts have been taken in the last decade to develop an improved vaccine. The Modified-Vaccinia-Ankara (MVA) 85A vaccine was one among them.[15] However, further clinical trials, and studies have shown that it has not sufficed in providing better protection against TB. The need for a better vaccine is evident; however, limitations in our knowledge of which aspects of BCG immunity are important for long-lasting protection against MTB prevent successful efforts.

TB remains a prominent global health issue and the rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) (MDR with added resistance to a fluoroquinolone and an injectable second line agent) strains, and the lack of new effective drugs is of major concern.[16] M. Tuberculosis develops drug resistance exclusively through chromosomal mutations, in particular single-nucleotide polymorphisms and a few through gene environment interaction.[17] However, the recent application of genetic techniques provides a promising avenue. Using whole-genome sequencing, comparative genomics and systems biology are useful techniques to understand the origin and ongoing evolution; and molecular basis of M. Tuberculosis.[17] Prominent research in this direction is to further understanding of our perspective of the TB, development of new vaccines and drugs, and treatment of patients using existing regimens.

Additionally, previous treatment, not complying with treatment, not completing treatment and improper or inadequate regimens can also confer drug resistance.[11,13,18] According to the WHO Global tuberculosis report 2014, 136,000 cases eligible for MDR-TB treatment was detected in 2013, up from 52,825 cases detected in 2009. The number of MDR-TB cases enrolled on treatment went up from 30, 500 in 2009 to 97,000 in 2013. Drug resistance continues to pose a major health concern. A recent analysis of trends focussed on the period 2008−2013 suggests that globally, the estimated proportion of new cases with MDR-TB has not changed and remains at about 3.5%, where most cases found in India, China, and Russia.[18]

CONTROL OF TB

Recent WHO reports have shown that some countries, like Cambodia, have shown a drastic decline in the number of TB cases. Treatment regimens and innovative diagnostic tools have saved approximately 37 million lives in the last decade.[19] Even today the major obstacle in conquering TB is due to complication posed by MDR, XDR, HIV and the inefficacy of the BCG vaccine, non-compliance to treatment and the lack of development of better and newer drugs and vaccines.

Developing countries like India, China, and Russia, TB rates have shown a decline, but the curve is really low.[13] Directly observed therapy short-term (DOTS), which closely monitors treatment adherence and completion[10] has been useful in these countries with large populations. The main goal of DOTS is to increase efficiency and cost-effectiveness in developing nations.[12] DOTS-plus was initiated recently to to tackle MDR-TB and proves to be a more rigorous treatment strategy.[12,19]

In 2006, WHO developed a six point Stop TB Strategy. The main goal of this strategy is to reduce the global burden of tuberculosis by 2015 by ensuring all TB patients (those co-infected with HIV and those with drug-resistant TB) benefit from universal access to high-quality diagnosis and patient-centered treatment. The strategy also supports the development of new and effective tools to prevent, detect and treat TB. The Stop TB Strategy underpins the Stop TB Partnership's Global Plan to Stop TB 2006-2015.[20]

CONCLUSION

Tuberculosis still remains a global public health burden, despite extensive measures for the prevention and treatment strategies. Early diagnosis and treatment planning may help in preventing complications and death resulting due to this common infectious multi systemic disorder.

REFERENCES

1. Kolokotronis A, Antoniadis D, Trigonidis G, Papanagiotou P. Oral tuberculosis: Oral Dis 1996;2:242-243.
2. www.tbc India.nic.i
3. Smith KC, Armitige L, Wanger A. A review of tuberculosis: reflections on the past, present and future of a global epidemic disease. Expert Rev Anti Infect Ther 2003; 1(3): 483-491

4. Eng HL, Lu Sy, Yang Ch, Chen WJ. Oral Tuberculosis. Oral Surg Oral Med Oral Radiol Endod.1996;81:415–20
5. Umadevi M, Ranganathan K, Saraswathi TR, Uma R, Elizabeth J. Primary Tuberculous Osteomyelitis of the Mandible. Asian J Oral Maxillofac Surg. 2003;15:208–13.
6. Shafer WG, Hine MK, Levy BM. Bacterial Infection of the Oral Cavity. In: Shafer WG, Hine MK, Levy BM, editors. Textbook of Oral Pathology. 6th Ed. Philadelphia: W.B. Saunders Company; 2011. Pp. 313–7.
7. Raj Neelam, Sahoo Subhas, V. Ram Mohan Gupta, Devanna N, Pati Nikunja B. A review on new approaches and current therapies involved in the treatment and prophylaxis of tuberculosis. Int. Res. J. Pharm. 2012; 3 (12): 46-50
8. Erbaycu AE, Taymaz Z, Tuksavul F, Afrashi A, Güçlü SZ. "What happens when oral tuberculosis is not treated?". Monaldi Arch Chest Dis 2007;67:116-8
9. Greenberg MS, Glick M. In: Burket's Oral Medicine Diagnosis and Treatment 10th ed. New York: BC Decker, 2003.
10. Hasan S, Khan MA. Tuberculosis - A common disease with uncommon oral features Report of two cases with a detailed review of literature. Proceedings of the World Medical Conference. Prague 2011; 156-164.
11. Cruz-Knight, W, Blake-Gumbs, L. Tuberculosis**:** an overview**.** Prim Care. 2013; 40: 743–756
12. Goldman, L., Schafer, A.I. Tuberculosis: disease overview. In: L. Goldman, A.I. Schafer (Eds.) Goldman's Cecil medicine: expert consults premium edition. 24th Ed. Saunders Elsevier, St. Louis (MO); 2011
13. Mason, R.J., Broaddus, V.C., Martin, T.R., King, T.E., Schraufnagel, D.E., Murray, J.F., and Nadel, J.A. Tuberculosis. In: J.F. Murray, J.A. Nadel (Eds.) Murray and Nadel's textbook of respiratory medicine. 5th Ed. Saunders Elsevier, St. Louis (MO); 2010
14. Ranaivomanana P, Raharimanga V, Dubois PM, Richard V, Rasolofo Razanamparany V. Study of the BCG Vaccine-Induced Cellular Immune Response in Schoolchildren in Antananarivo, Madagascar. PLOS ONE 2015; 10 (7): e0127590.
15. Andersen P, Woodworth, J.S. Tuberculosis vaccine – rethinking the current paradigm. Trends Immunol. 2014; 35: 387–395
16. James E. Galagan. Genomic insights into tuberculosis, Nature Reviews Genetics 2014; 15: 307-320
17. World Health Organization, Global Tuberculosis Report (WHO 2014)
18. World Health Organization. (c1948. Tuberculosis fact sheet) in: Geneva (Switzerland): WHO global TB program.
19. Nicole Fogel, Tuberculosis: A disease without boundaries, Tuberculosis (Edinb). 2015 Jun 25.
20. World Health Organization, The Stop TB Strategy (WHO 2006)

Cite this article as:

Shazina Saeed, Shamimul Hasan. Tuberculosis: A public health challenge: brief overview of literature. Int. Res. J. Pharm. 2016;7(1):1-4 http://dx.doi.org/10.7897/2230-8407.0711

Source of support: Nil, Conflict of interest: None Declared