Short Communication

iMedPub Journals
http://www.imedpub.com

Journal of Molecular Biology and Biotechnology

2017
Vol. 2 No. 1: 1

Pathogenic Aspects of Genito-Urinary Tuberculosis in Males and Females

Laxman S Meena and Ramiza Ansari

CSIR-Institute of Genomics and Integrative Biology, Council of Scientific and Industrial Research, Mall Road, Delhi, India

Corresponding author: Laxman S Meena

meena@igib.res.in, Laxmansm72@yahoo.com

CSIR-Institute of Genomics and Integrative Biology, Council of Scientific and Industrial Research, Mall Road, Delhi-110007, India.

Tel: 011-27666156
Fax: 011-27667471

Citation: Meena LS, Ansari R. Pathogenic Aspects of Genito-Urinary Tuberculosis in Males and Females. J Mol Biol Biotech. 2017, 2:1.

Abstract

Tuberculosis (TB), one of the deadliest diseases is creating an impediment in human health world widely. *Mycobacterium tuberculosis* causes pulmonary TB, which later on shifts its impact on other body organs rather than only lungs. So here bacilli generate the extra-pulmonary form of TB. Genito-urinary form of EPTB is world's second most risky form of TB which brings ill effects on reproductive health of population. GUTB is much more destructive which affects males and females both but in males, susceptibility towards disease is more. Now-a-days infertility is the major concern in both males and females which arises due to the infection of bacilli in genital organs. Some frequent symptoms like dysuria, pyuria, abdominal pain, hematuria may be observed and fever, weight loss, anorexia are less common. GUTB can be diagnosed on the basis of various culture studies and also through the radiological imaging by ultra sound, pelvic MRI etc. PCR is also best method for the diagnosis of the bacilli of MTB in urine and the ideal result can be obtained within 24-48 hours. Surgery is also preferred if kidney or epididymis is infected with the bacilli.

Keywords: Genito-urinary tuberculosis; *Mycobacterium tuberculosis*; Fallopian tube; Seminal vesicles; Infertility; Male genital tuberculosis

Abbreviation: TB: Tuberculosis; MTB: *Mycobacterium tuberculosis*; EPTB: Extra pulmonary TB; GUTB: Genito-urinary tuberculosis; MDR: Multi drug resistance TB; XDR: Extensively drug resistance TB; TDR: Total drug resistance TB

Received: February 03, 2017; **Accepted:** February 15, 2017; **Published:** February 22, 2017

Introduction

Tuberculosis (TB), a contagious disease has affected people all over the world and is leading cause of death [1]. Although, most people are infected with this bacilli but only 5-10% people have chances to be ill with active TB. Patients affected with TB, if co-infected with HIV virus weakens the immune system which enhances the rate of active TB [2]. It is estimated that around 10.4 million new TB cases found in 2015 with 1.2 million people affected with HIV Positive. Among all of the above, 90% of cases were adults and 10% were children [3]. The emergence of Multi Drug Resistance (MDR), Extensively Drug Resistance (XDR) and Total Drug Resistance (TDR) in TB has led to TB crisis. Various approaches are needed to discover the superior diagnostic methods, treatments and vaccines to eradicate TB infection [4].

Mycobacterium tuberculosis (MTB) is the aerosolized etiological agent of this disease which is an obligate and opportunistic parasite that usually infects lung macrophages [5]. During initial infection of TB, bacilli are engulfed by the alveolar macrophages in the lungs, where it replicates and initiates the host immune system [6]. The bacilli can also infect the non-phagocytic cells including M cells, Type I and Type II epithelial cells (pneumocystis) etc. [7]. The entry of bacilli leads to create difference in signal transduction and immune activation [8-10]. During infection various surface antigenic molecules that are secreted by MTB are involved in the modulation of host immune response [11]. During the time of host pathogen interaction various proteins are also required like Fcγ receptors, Complement receptors, mannose receptors etc. which helps in the acquisition of MTB and also toll like receptors are involved in the recognition of MTB [12]. Some of the antigenic proteins are also released in small membranous vesicles which are considered as the transporter of virulent proteins and also helps in immune modulation [13] **(Figure 1).**

Broadly TB can be categorised into two forms i.e., Pulmonary TB, a pestilential bacilli infection that mainly affects lungs and is

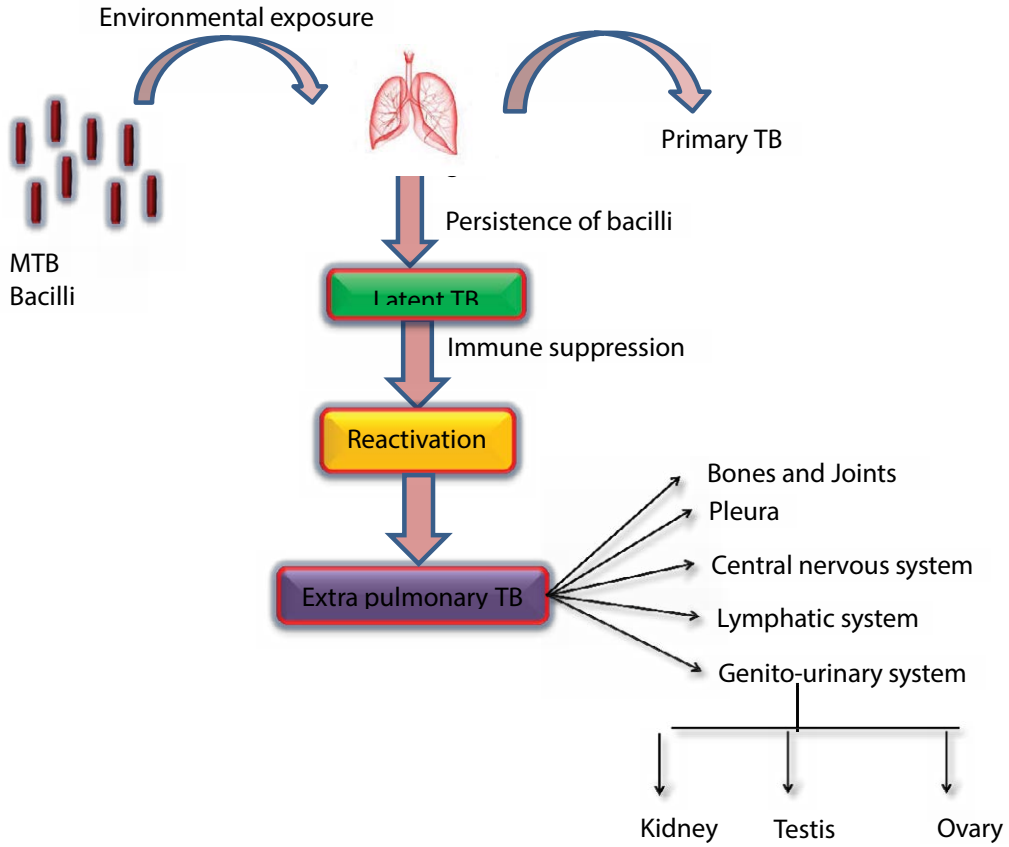

Figure 1 Graphical representation of emergence of genital urinary tuberculosis.

usually self-limited [14] and Extra pulmonary TB (EPTB), where the bacilli infects other parts of body apart from lungs via blood stream [15]. Generally, the risk of EPTB increases with immune-suppression [16]. In EPTB, various locations are affected like joints, bones, pleura, genito-urinary tract etc. Among all genito-urinary tracts kidney is the most common site of infection of EPTB [17].

Genito-Urinary Tuberculosis

Genitourinary tuberculosis (GUTB) is the 2nd most form of EPTB which was coined by Wildboltz in 1937 [18]. The infection and incidence rate of GUTB shows devastating effect mostly in the people of developing countries [19]. About 2-20% chances are there that the patient with pulmonary TB can have GUTB. The term GUTB includes kidney TB, male and female genital TB and urinary tract TB [20]. Because of no specific signs and symptoms there is delay and difficulty in diagnosis and treatment of the disease which leads to mortality [21,22]. GUTB results from primary infection or by the reactivation of the initial infection. GUTB is more common in men than in women in the ratio of 2:1. Some authors found that kidney failure is very less commonly seen and mainly affects the lower genitourinary system which includes epididymis, seminal vesicles, prostate, scrotum are affected in males [23] similarly fallopian tubes, ovaries, endometrium, cervix, myometrium, vulva are affected in females [24].

Pathogenic Aspects of GUTB

In GUTB the bacilli reach the genital tract usually through haematogenous route, lymphatic spread or the direct spread [25]. The bacilli can also transfer during the sexual intercourse with the partner suffering from TB lesions of genitilia [26]. Mucosal genitilia is generally of two types: Type I mucosal surface and Type II mucosal surface.

The female genital tract is composed of type I (endocervix and uterus) and type II (outer vagina, inner vagina, ectocervix) genitalia [27]. Dysfunction of menstruation, pregnancy loss, pelvic pain etc. may be usual presentation under female GUTB with physical, psychological and social effects [28]. But the women who are suffering from post-menopause have very rare chances of attainment of this disease. Infertility is a leading sign of patients suffering from GUTB and 94% of women with GUTB have affected their fallopian tubes, endometrium and cervix [29]. The fallopian tube gets thickened and shows a rough external surface with adhesions [30]. Inflammation of fallopian tubes i.e., salpingitis results from haematogenous infection. TB salpingitis can cause peritonitis, endometriosis, cervicitis and vaginitis [31]. Therefore it is also considered that GUTB is a probable cause for the infertile couples mainly in the population of high prevalence of TB [32]. Even after the treatment of this disease, there is very less chances of successful pregnancy and the rate of live birth

is very low [33]. Also, the bacilli have the ability to destroy the ovaries completely. Foetus also gets affected with TB infection from the mother through umbilical vein to fetal liver via placental TB [34]. In this context, to achieve successful pregnancy there is need of *in vitro* fertilisation with embryo transfer.

In males, genitalia are composed of external and internal genitalia [35]. TB with the involvement of the prostate and seminal vesicles are usually secondary to infection from the upper genitourinary tract and may cause a variety of changes such as necrosis, calcification, caseation, and cavitation [36]. It is also seen that the men with genital TB have high chances of radiological abnormalities in the urinary tract so it is necessary to investigate the urinary tract [37]. Epididymis is considered as one of the ideal site of TB infection [38]. The TB patient with the infection of genital tract has the primarily involvement of the infertility which usually occurs in the reproductive age group. Tuberculous infection of the seminal vesicles or the prostate may be diffuse and result in aspermia without a demonstrable obstruction of the ejaculatory ducts [39].

Diagnostic Approaches

GUTB can be diagnosed by the help of Polymerase Chain Reaction (PCR) mainly for the bacilli of MTB which is present in urine and the ideal result can be obtained within 24-48 hours [40]. Also the patient prefer for surgery in which the kidney or epididymis which is infected with the bacilli is removed out [41]. Some of the advanced tests to diagnose the GUTB are Mycobacterial smear and culture test, Nucleic acid amplification test, Interferon γ release assay (IFN- γ), radiographic imagining, intravenous urography and cystoscopy etc. IFN- γ assay has sensitivity of 84-95% ans specificity of 85-99%. This data makes it most authentic assay to deduce the pathogenicity of GUTB. It is an *in vitro* test for quantitative analysis of the IFN- γ response to antigens representing Mtb such as ESAT-6 (Early secretory antigenic target) [42]. MB Bac T liquid culture and Accu Probe identification system provide the most reliable and quick diagnostic proofs towards the disease. In different assays, sensitivity profile is enhanced by major factor by using PCR [43]. The treatment is the same as in the case of pulmonary TB but the early diagnosis of infection is more important here.

Management

In GUTB drug treatment first line therapy is normal course of drug regimen. In the course of a follow-up of more than 40 years, the treatment time was reduced from 24 months to 6 months. A 6-month short course of anti-tuberculous drug regimen is effective in uncomplicated GUTB. All patients with GUTB should be evaluated for concomitant involvement of the lungs as well as other organs [43]. The analysis of symptoms such as cough expectoration, hemoptysis and dyspnea followed by a chest radiograph and examination of at least three sputum smears for acid fast bacilli is the least evaluation for pulmonary association necessary in all patients with GUTB. If present, the probabilities of drug resistance of TB is greater, and category second DOTS would be the suitable management [44]. The major determinant of the outcome of treatment is patient adherence to the drug regimen. Diagnosis of genital TB is still a difficult task to do and most of the patients are misdiagnosed. So, we need an early and reliable detection procedure by which the infection can be controlled.

Summary

GUTB is the worldwide disease which has much destructive feature like the non-functioning of kidney, renal failure, infertility etc. Male and female genital organs both are affected and diagnosis can be done on the basis of culture studies and also through the radiological imaging by ultra sound, pelvic MRI etc. PCR can also be used to diagnose the bacilli which are present in urine within very short period of time. The two most significant aspects of efficiency of any blend schedule for the treatment for the GUTB are, rapid and complete killing of the bacillary residents resulting in cure and prevention of waning following successful cure. GUTB affected majorly the infertility in humans which is becoming a major concern in the field of fertility. So, we need a fast and progressive approach to handle the disease consequences. It requires extensive research to know the pathological aspect of GUTB.

Acknowledgement

The authors acknowledge financial support from GAP0092 of the Department of Science and Technology and OLP1121 of the Council of Scientific and Industrial Research.

Conflict of interest

There is no conflict of interest.

References

1 Meena LS, Rajni (2010) Survival mechanisms of pathogenic *Mycobacterium tuberculosis* H_{37}Rv. FEBS J 277: 2416-2427.

2 Meena LS, Chopra P, Bedwal RS, Singh Y (2008) Cloning and characterization of GTP-binding proteins of *Mycobacterium tuberculosis* H_{37}Rv. Enzyme Microb Techno 42: 138-144.

3 http://www.who.int/tb/publications/global_report

4 Kulchavenya E, Dubrovina S (2014) Typical and unusual case of female genital tuberculosis. ID Cases 1: 92-94.

5 Lamprecht DA, Finin PM, Rahman MA, Cumming BM, Russell SL, et al. (2016) Turning the respiratory flexibility of *Mycobacterium tuberculosis* against itself. Nat commun 7: 12393.

6 Meena PR, Monu, Meena LS (2015) Fibronectin binding protein and Ca^{2+} play an access key role to mediate pathogenesis in *Mycobacterium tuberculosis*: An Overview. Biotechnol Appl Biochem 63: 820-826.

7 Muttarak M, ChiangMai WN, Lojanapiwat B (2005) Tuberculosis of the genitourinary tract: Imaging features with pathological correlation. Singapore Med J 46: 568-575.

8 Jacobs AJ, Mongkolsapaya J , Screaton GR, McShane H, Wilkinson RJ (2016) Antibodies and Tuberculosis. Tuberculosis (Edinb) 101: 102-113.

9 Norazmi MN (2013) Pattern recognition receptors and cytokines in Mycobacterium tuberculosis infection-the double-edged sword. Biomed Res Int 1-18.

10 Arruda S, Bomfim G, Knights R, Huima-Byron T, Riley LW (1993) Cloning of an M. tuberculosis DNA fragment associated with entry and survival inside cells. Science 261: 1454-1457.

11 Rajni, Rao N, Meena LS (2010) Biosynthesis and virulent behaviour of lipids produced by *Mycobacterium tuberculosis*: LAM and Cord factor: An overview. Biotechnol Res Int 2011: 1-7.

12 Crevel RV, Ottenhoff THM, Van der Meer JWM (2002) Innate immunity to *Mycobacterium tuberculosis*. Clin Microbiol Rev 15: 294-309.

13 Al-Nedawi K, Meehan B, Rak J (2009) Microvesicles: Messengers and mediators of tumor progression. Cell Cycle 8: 2014-2018.

14 Figueiredo AA, Lucon AM (2008) Urogenital tuberculosis: Update and review of 8961 cases from the world literature. Rev Urol 10: 207-217.

15 Hsu CW, Hu SC, Hsu YH, Liu SW (2008) Genital tuberculosis with presentation of spontaneous abortion in a patient with miliary tuberculosis. Tzu Chi Med J.

16 Chaves AS, Rodrigues MF, Mattos AMM, Teixeira HC (2015) Challenging *Mycobacterium tuberculosis* dormancy mechanism and their immunodiagnostic potential. Braz J Infect Dis 19: 636-642.

17 Zarrabi AD, Heyns CF (2009) Tuberculosis of the urinary tract and male genitalia – a diagnostic challenge for the family practitioner. S Afr Fam Pract.

18 Abbara A, Davidson RN (2011) Etiology and management of genitourinary tuberculosis. Nat Rev Urol 8: 678-688.

19 Kandola P, Meena LS (2013) Extra pulmonary tuberculosis: Overview, manifestations, diagnostic and treatment techniques. Adv Mater 1: 13-19.

20 Figueiredo AA, Lucon AM, Junior RF, Srougi M (2008) Epidemiology of urogenital tuberculosis. Int J Urol 15: 827-832.

21 Kulchavenya E (2014) Urogenital tuberculosis: definition and classification. Ther Adv Infect Dis 2: 117-122.

22 Merchant S, Bharati A, Merchant N (2013) Tuberculosis of the genitourinary system-Urinary tract tuberculosis: Renal tuberculosis-Part I. Indian J Radiol Imaging 23: 46-63.

23 Kulchavenya E (2016) Urogenital tuberculosis as a part of extrapulmonary tuberculosis: Epidemiology and some aspects of diagnosis and therapy. Novosibirsk Medical University, Russia.

24 Sharma JB (2016) Sharma's python sign: A new tubal sign in female genital tuberculosis. J Lab Physicians 8: 120-122.

25 Das P, Ahuja A, Gupta SD (2008) Incidence, etiopathogenesis and pathological aspects of genitourinary tuberculosis in India: A journey revisited. Indian J Urol 24: 356-361.

26 No Authors Listed (2015) TB and infertility- conceive after having genital tuberculosis.

27 Goel G, Khatuja R , Radhakrishnan G, Agarwal R , Agarwal S, et al. (2013) Role of newer methods of diagnosing genital tuberculosis in infertile women. Indian J Pathol Microbiol 56: 155-157.

28 No Authors Listed (2015) UNDP discussion paper: Gender and TB.

29 Eryani AAA, Abdelrub AS, Harazi AHA (2015) Genital tuberculosis is common among females with tubal factor infertility. AJM 51: 321-324.

30 Botha MH, Van der Merwe FH (2008) Female genital tuberculosis. SA Fam Pract 50: 12-16.

31 Arora VK, Gupta R, Arora R (2003) Female genital tuberculosis-need for more research. Ind J Tub 50: 9.

32 Neonakis IK, Spandidos DA, Petinaki E (2011) Female genital tuberculosis: A review. Scand J Infect Dis 43: 564-572.

33 Kulchavenya E, Felker I, Brizhatyuk E (2014) International Conference "Urogenital infections and tuberculosis" in Novosibirsk, Russia, has opened new perspectives in the fight against tuberculosis. Antibiotics (Basel) 3: 121-127.

34 Ormerod P (2001) Tuberculosis in pregnancy and the puerperium. Thorax 56: 494-499.

35 Gibson MS, Puckett ML, Shelly ME (2003) Renal tuberculosis. Radiographics 24: 251-256.

36 Kulchavenya E, Kim CS, Bulanova O, Zhukova I (2012) Male genital tuberculosis: Epidemiology and diagnostic. World J Urol 30: 15-21.

37 Lima NA, Vasconcelos CC, Filgueira PH, Kretzmann M, Sindeaux TA, et al. (2012) Review of genitourinary tuberculosis with focus on end-stage renal disease. Rev Inst Med Trop Sao Paulo 54: 57-60.

38 Stepanov PI (2014) Actual issues of pathogenesis of tuberculosis of male genital organs. Urologia 2: 36-39.

39 Kumar R (2008) Reproductive tract tuberculosis and male infertility. Indian J Urol 24: 392-395.

40 Jindal UN, Bala Y, Sodhi S, Verma S, Jindal S (2010) Female genital tuberculosis: Early diagnosis by laparoscopy and endometrial polymerase chain reaction. Int J Tuberc Lung Dis 14: 1629-1634.

41 Lessnau KD (2011) Tuberculosis of the genitourinary system overview of GUTB. Medscape 450651.

42 Shenoy VP, Chkradhar V, Munim F, Mukhopadhyay C (2014) An integrated approach using liquid culture system: Can it make an impact for clinical diagnosis of genitourinary tuberculosis? AMHS Res.

43 Kadhiravan T, Sharma SK (2008) Medical management of genitourinary tuberculosis. Indian J Urol 24: 362-368.

44 Sia IG (2011) Wieland ML: Current concepts in the management of tuberculosis. Mayo Clin Proc 86: 348-361.