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A Review Article on Tuberculosis

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ABSTRACT

Tuberculosis remains one of the deadliest infectious diseases responsible for millions of deaths annually across the world. Tuberculosis is an ancient disease with high incidence and mortality rates in Africa and Asian countries. This can be because of multidrug resistant (MDT) TB. Extensively drug resistant TB and human immunodeficiency virus. Mycobacterium tuberculosis and other closely related strains is the major cause of tuberculosis. M .tuberculosis develops resistant to most antitubercular drugs in use .Tuberculosis is still a leading cause death worldwide almost a third of the world's population is infected with TB bacilli and each year approximately 8 million people develop active. Tuberculosis. However there are few studies of long term treatment outcomes from directly observed. Therapy short courses programs in high burden settings and particularly settings of the high drug resistance. This study is systematic review to evidence the incidence and prevalence of latent TB infection and disease. .Patients new and retreatment TB cases who received short course chemotherapy with isoniazid, rifampicin, pyrazinamide and either Ethambutol or streptomycin between 1994 and 1996.

Keywords: Diagnosis, Antibiotic, Antimicrobial , Mycobacterium Tuberculosis.

1. INTRODUCTION

Tuberculosis (TB) is an infectious disease usually caused by Mycobacterium tuberculosis (MTB) bacteria. Tuberculosis generally affects the lungs, but it can also affect other parts of the body.[1]

Tuberculosis (TB) is a potentially serious infectious disease that mainly affects the lungs. The bacteria that cause tuberculosis are spread from person to person through tiny droplets released into the air via coughs and sneezes [2] .Tuberculosis (TB) has consistently shown a much higher annual mortality rate than HIV or any other infection. This is due to an array of events that begins with the virulence of Mycobacterium tuberculosis, the highly contagious and persistent bacterium responsible for TB infection [3]It is the second leading cause of death from an infectious disease worldwide after the human immunodeficiency virus (HIV) [4] There were an estimated 13.7 million chronic active cases globally in 2007, while 8.8 million new cases and 1.5 million associated deaths were reported in 2010, mostly occurring in developing countries [5]. In 2011, TB was the foremost death causing infectious disease worldwide after HIV and liable for 1.7million deaths [6]. Although 80 percent of the population of Asian and African countries showed positive tuberculin tests, only 5-10 percent people of United States are diagnosed positive with this test. This shows heterogeneous distribution of tuberculosis across the globe [7]. The data released by the World Health Organization (WHO) in November 2010 shows continuous fall in number of new cases of TB globally in five out of six WHO regions. According to latest reports of WHO, 8.6 million people were suffering from TB in 2012 and 3 million of them were not diagnosed and thus not treated [8,9] The World Health Organization (WHO) has published a global TB report every year since 1997. The purpose of the report is to provide a up-to-date the status of the TB epidemic, and of progress in the response to the epidemic – at global, regional and country levels . [10]

2. ETIOLOGY OF TUBERCULOSIS -:

Mycobacturium tuberculosis–most common cause Other than tuberculosis-includes:

a. M. avium Complex (MAC)

b. M. kansasii

c. M. scrofulaceum

d. M. marinum

e. M. ulcerans

f. M. fortuitum

g. M. chelonei [11]

3.TYPES OF TUBERCULOSIS -:

TB can be active or latent.

3.1] Active TB

In Active TB presence of germs in our body. This germs multiply and make sick . person can spread the disease to others.mostly active tb cause by reactivation of latent tb

But general symptoms of active TB include:

- Unexplained weight loss
- Loss of appetite
- Fever
- Chills
- Fatigue

Active TB can be life-threatening if not properly treated.

3.2] Latent TB

If you have latent TB infection, you have TB bacteria in your body, but it's inactive. This means you don't experience any symptoms. You also aren't contagious. Still, you'll have a positive result from TB blood and skin tests.

Latent TB can turn into active TB in 5 to 10 percent of people. This risk is higher for those with a weakened immune system due to medication or an underlying condition. [12,13]

3.3] Pulmonary TB

Pulmonary TB is active TB that involves the lungs. It's likely what most people think of when they hear tuberculosis .Along with the general symptoms of TB, a person with pulmonary TB may also experience:

- persistent cough lasting three week
- coughing up blood
- coughing up phlegm
- chest pain
- shortness of breath

3.4] Extrapulmonary TB

Extrapulmonary TB is TB that involves parts of the body outside of the lungs, such as the bones or organs. Symptoms depend on the part of the body affected [14] Extrapulmonary involvement can be seen in more than 50 percent of patients with concurrent AIDS and tuberculosis.[15,16,17] The risk of extrapulmonary tuberculosis and mycobacteria increases with advancing immunosuppression [18]

4. PATHOPHYSIOLOGY OF TUBERCULOSIS-:

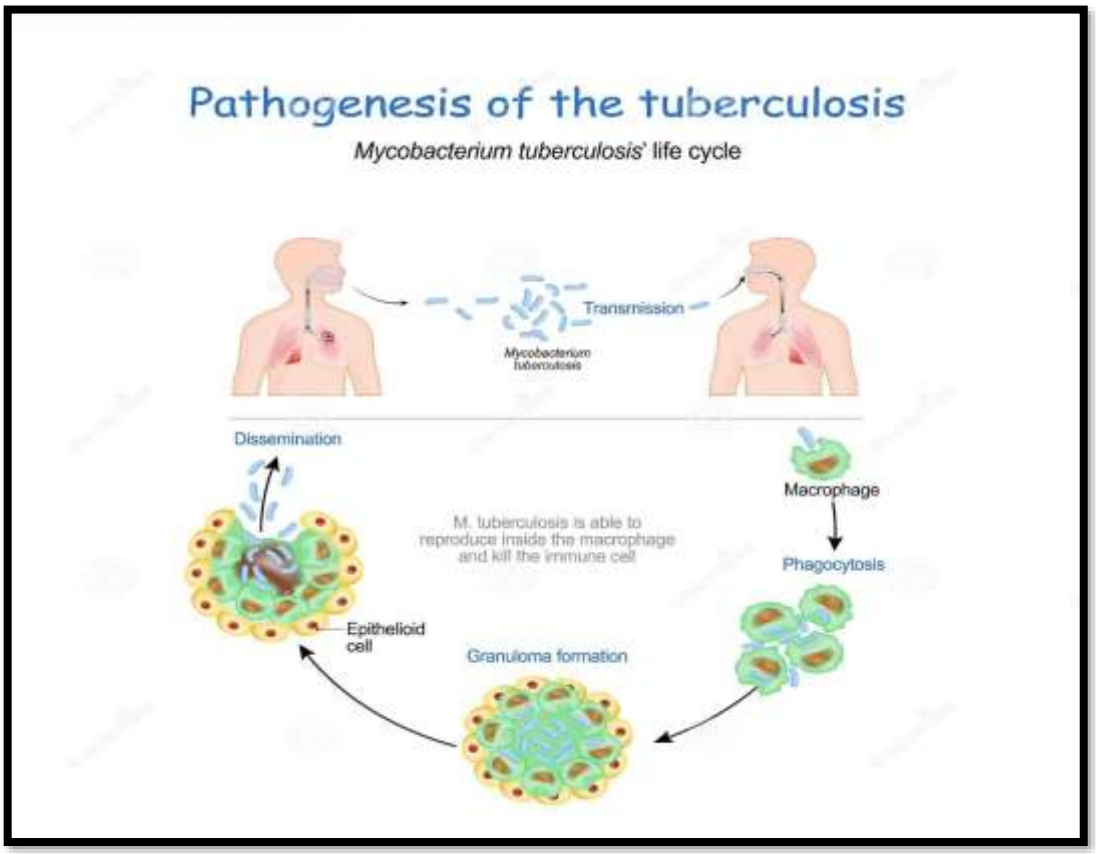
Tuberculosis infection begins with when TB infected individual cough, sneeze, then droplets spread in air and its inhales by person.

Then mycobacteria reaches to alveolar air sac of lung and then replicate and activate immune response involving alveolar macrophages are combat with infection by phagocytosis, inhibit the host bacteria multiplication[19] or progress for active TB called primary progressive tuberculosis. depend on strength Of patient.

After swalled by macrophages, bacteria continue to multiply slowly with cell division occurs every 1-2 day. Then it cause production of proteolytic enzyme and cytokines by macrophages to degrade bacteria. microorganism continue to grow until they reach adequate number to fully provoke cell-mediated immune response. It is detect by skin test called **tuberculine skin test.** [20]

Then form granuloma with lymphocytes surrounded by infected macrophages. bacteria present inside granuloma cause infection and then necrosis occurs.[21] .

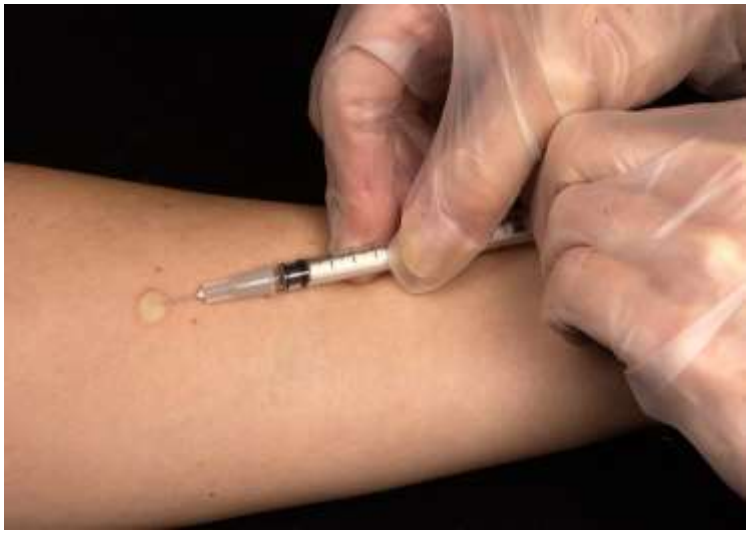
Fig number 1- (pathophysiology of Tuberculosis)



5. DIAGNOSIS

5.1. Tuberculin test - is used to confirm infection. Two tests are commonly used. They are (A) Heaf (multiple puncture) test and (B) Mantoux test Mantoux Test: A Mantoux test is a skin test for tuberculosis. Here, an extract that is made from dead mycobacterium is injected right under the surface of the skin. This injection leads to an allergic response characterised by swelling, redness and firmness of the injected area. The presence of all three of these in a significant manner is a positive test.. If there is no firmness or redness, the test is negative.(22)

Fig number _2 Tuberculin test.



5.2. Blood test -:

It helps to indentify TB. It measures immune system reaction to bacteria.

There are two test _

- T – SPOT TB TEST (T- SPOT)

It based on enzyme linked immunespot (ELISPOT) method, detect number of IFN- Gamma producing cell after mtb- specific antigen stimulation.

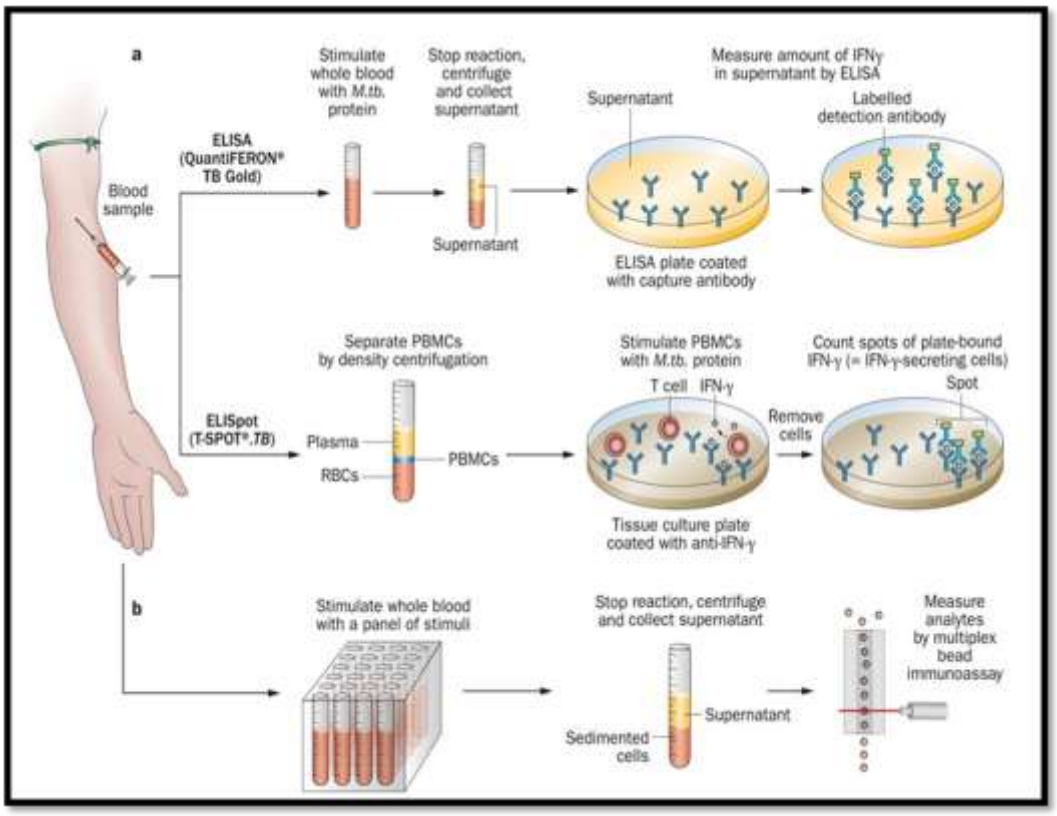
Useful in diagnosis of extrapulmonary TB.

- QUANTIFERON – TB GOLD in tube test (QFT- GIT)

A QFT assay is based on the enzyme linked immunosorbent assay to detect IFN- Gamma Secreted into the supernatant of culture medium after Mtb-specific antigen stimulation.The advantages and limitations of QFT are similar to those of T-SPOT. (23)

Fig number _ 3

Blood test



5.3. Chest X-Ray:

A chest x-ray is a very useful test in the diagnosis of pulmonary tuberculosis. A lot of times, however, the chest x-ray can be normal. In those who have active tuberculosis, there can be present patches in the upper part of the lung (24)

5.4. Microscopy:

Use for active TB disease diagnosis. Direct visualisation of mycobacteria using microscopy. (25) Sputum smear microscopy – is discovered by two German doctor, Franz – ziehl and Friedrich Nielsen. Its test for tb bacilli.(26)

5.5. Nucleic acid amplification (NAA) tests

These techniques comprise to polymerase chain reaction (PCR), Amplicon MTB Test (Roche Diagnostic Systems Inc. New Jersy, USA), and the amplified MTB Direct Test (MTD, Gen- Probe, California, USA). The PCR device is based on identifying the Species- specific DNA segments of the TB bacillus

from a given Sample. The Amplicon is a DNA founded test that amplifies and Expose the presence of a specific ribosomal RNA of TB bacilli in a Colorimetric reaction. The MTD test is founded on the amplification Of the same ribosomal RNA of the TB bacilli but its detection is with A DNA probe. These principal confirm the presence of M. TB within 1-3 days. These principal are being used to identify MDR-TB as Mutations in the DNA of MTB, which confer the drug resistance, Have been discovered.

5.6. Tuberculin Skin Testing (TST)

TST is a classical method based on detection of type IV hypersensitivity using purified Protein derivative (PPD) of tuberculin. Mtb-infected patients can produce sensitized T Lymphocytes with the ability to recognize Mtb antigens. When the sensitized T lymphocytes Are stimulated by Mtb antigens again, a variety of soluble lymphokines are released to Increase the vascular permeability, local redness, swelling, and induration (27,28)

5.7. Urine test_:.

If bladder is affected by tb then pus is occurs .

6. TREATMENT OF TUBERCULOSIS :

the treatment of tuberculosis patients in India, two categories need to be considered. One category is those who have had no diagnosis of tuberculosis ever made and are taking treatment for the first time. The second category is those who have previously received treatment for tuberculosis and are having a recurrence.

In those with a new diagnosis, the primary treatment regimen consists of a combination of drugs. This includes .

6.1 CLASSIFICATION OF DRUGS:

A] First line drug:

These drugs have high anti tubercular efficacy as well as low toxicity; are used

1) Isoniazid (H)

2) Rifampin

3) Pyrazinamide (Z)

4) Ethambutol (E)

5) Streptomycin(S)

B] Second line drug:

These drugs have either low anti tubercular efficacy or high toxicity or both are used in

special circumstances only.

1) Thiacetazone (Tzn)

2) Para amino salicylic acid (PAS)

3) Ethionamide (Etm)

4) Cycloserine (Cys)

5) Kanamycin (Kym)

6) Amikacin (Am)

7) Capreomycin (CPR)

These are initially given for a period of 2 to 3 .

6.2 DOTS (directly Observed treatment, short-course)_:

which includes specific Combinations of anti-TB medicines, is another strategy Developed by World Health Organization (WHO) to control tuberculosis (29), all patients receive their daily tuberculosis medicines under a protocol called directly observed therapy short term or DOTS. Here, a volunteer or a member of the family watches the patient take their medication regularly without fail. This is to ensure that the treatment that is given is followed religiously and patients do not miss any doses as this can be harmful.

There remains an entity called multidrug-resistant tuberculosis where all the medications prescribed do not work. These people require specialised input from experts in tuberculosis management and often require injections on a regular basis to help cure tuberculosis.

Multidrug-resistance (MDR) is mainly concerned with The resistance of M. tuberculosis strains to both isoniazid and Rifampicin, regardless of the sensitivity/resistance to other Drugs. MDR-TB is alarming due to the high risk of death Associated with it while resistance to either drug may be Managed with other first-line drugs or second-line drugs Under DOTS Plus. (30)

Table number 1_ classification of antitubercular drugs

FIRST LINE DRUG	Reference number	MOA	DOSE	SIDE EFFECT
1] ISONIAZID	31	Block synthesis of mycolic acid is component of mycobacterial cell wall.it required for growth of mycobacteria.	Single daily dose 4-5 mg/kg of body weight or 300mg oral i. M	Rashes, fever,Blurred vision or loss of vision, fever and sore throat, joint pain, skin rash.,.
2] RIFAMPICIN	32	It inhibit DNA dependent RNA synthesis.	Daily dose 10-12mg/kg body weight or 450-600mg oral, i. V qd.	Hepatitis, Respiratory syndrome, cutaneous syndrome, abdominal syndrome.
3] STREPTOMYCIN	33	Bind to 30s and 50s sub units of ribosomes as well as their interface, freeze initiation, interfere with polysome formation and cause misreading of mRNA code, thus inhibit protein biosynthesis.	Daily Dose 12_18 mg/ kg	Ototoxicity, Nephrotoxicity
2) SECOND LINE DRUGS :				
1] Para amino salicylic acid (PAS):	34	Inhibit the PABA in Corporation in to bacterial cell wall	10-12g per day in divided dose oral bid.or. tid	Anorexia, Nausea, Epigastric pain, rashes, fever, goiter
2] Ethionamide (Etm):	35	It is bacteriostatic against M. tuberculosis. It inhibits the synthesis of mycolic acid found in the bacterial cell wall, thereby inhibiting bacterial cell wall synthesis. It leads to bacterial cell wall disruption and causes cell lysis.	Dosing may initiated at 250 mg/day, and increased every 5–6 days to reach 750 mg/day (10–15 mg/kg/day)	Pain, Anorexia, nausea, vomiting, abdominal upset, rashes
3] Cycloserine [cys]	36	Inhibit Inhibit bacterial cell wall synthesis by inactivating the enzyme Which racemize Lalanine and link two Dalanine residues.	250- 500mg oral.	Pain,rashes, Vomiting

7. Tuberculosis Prevention:

There are many ways to prevent tuberculosis. In children, the tuberculosis vaccine is administered to prevent TB infection in the future. The vaccine is called the BCG vaccine or Bacille Calmette Guerin vaccine.

BCG vaccinations

BCG vaccine does not protect against infection. Instead it prevents the more serious forms of disease such as miliary tuberculosis and tuberculosis meningitiss.24The aim of BCG vaccination is to induce a benign artificial primary infection which will stimulate an acquired resistance to possible subsequent infection with virulent tubercle bacilli, and thus reduces the morbidity and mortality from primary tuberculosis risk.

Fig 4- BCG VACCINE

8. CONCLUSION

Tuberculosis is challenging health problem in developing countries. Increase in number of strains that are resistant to drug leads to multi and extensively drug resistant tuberculosis this resistance can be due to treatment failure , re- infection and co- morbidity with HIV/AIDS.

We conclude that tuberculosis infection and disease remain common in populations characterized by poor housing conditions. But Even though TB is an infectious disease it is curable if proper treatment and care are given so as to safeguard our newer generation from the shadow of this disease, they should be given BCG vaccines. Prophylactics measurement should be taken in order to prevent spread of the epidemic infection.Drugs such as isoniazid, Rifampicin ,ethambutol, pyrazinamide are used in treatment of the Tuberculosis.

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