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MARKET SURVEY OF ANTI- TUBERCULAR DRUGS

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Abstract

Given that molecular evidence for tuberculosis (TB) dates back over 17,000 years, it is one of humanity's oldest diseases. The fact that TB is among the top 10 infectious diseases that kill people worldwide, second only to HIV, despite advances in detection and treatment methods, is regrettable. The World Health Organization (WHO) asserts that TB is a global pandemic. It is one of the main reasons why persons with HIV pass away. If a patient contracts Multi-Drug Resistant Tuberculosis (MDRT), the process is extended to 24 to 28 months of Directly Observed Treatment with short course chemotherapy (DOTS) and other medications. It requires the right dose at least 6 to 8 months to cure TB.

Women's department of ONGC, school education, and integrated child development services (ICDS) are used to spread and sanitise society.Different treatment modalities are provided through the programme depending on the anti-microbial nature of the condition. Isoniazid-H, Rifampicin-R, Pyrazinamide-Z, and Ethambutol-E are the four first-line medications that are provided as a six-month, short course to new cases and those who don't show any signs of resistance

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KEYWORDS: MYCOBACTERIUM TUBERCULOSIS, RIFAMPICIN, PYRAZINAMIDE, ETHAMBUTOL, ISONIAZID

INTRODUCTION

Mycobacterium tuberculosis (MTB) germs typically cause the infectious illness tuberculosis (TB). Although it often affects the lungs, tuberculosis can also affect other body regions.body when an infection goes unnoticed for a long period of time, it is referred to as latent TB. In roughly 10% of cases, latent infections become acute diseases that, if untreated, kill about 50% of individuals who are infected. A persistent cough with blood-colored mucus, fever, night sweats, and weight loss are common signs of active TB. Due to the weight reduction, it was referred to as consuming in the past.

A wide variety of symptoms can result from infection in other organs. When persons with active TB in their lungs cough, spit, or otherwise release airborne particles, it spreads from one person to the next.Converse or sneeze Latent TB carriers do not disseminate the illness. More infections are active.frequently among smokers and persons with HIV/AIDS Chest X-rays are used to identify active TB.X-rays, microscopic analysis, and culture of bodily fluids are also used. Blood tests or the tuberculin skin test (TST) are used to diagnose latent TB.

As of 2018, it was estimated that latent TB infection affected one-fourth of the global population. Each year, 1% of the population develops new infections. With 1.5 million fatalities and an expected 10 million new cases of active TB in 2020, it will overtake COVID-19 as the second greatest cause of infectious death. By 2018, South-East Asia (44%), Africa (24%) and the Western Pacific (18%) were the regions with the highest rates of TB cases, with more than 50% of cases being identified in eight nations: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%) and Bangladesh (4%). There are fewer new cases every year now—about 2% fewer instances every year. Nearly 80% of those in several Asian and African nations, one-fourth of the population tests positive as of 2018, compared to 5–10% of Americans.Through the air, TB can transmit from one person to another. People who have lung TB cough, sneeze, or spit into the air, spreading the TB bacteria. Only a few number of these microbes must be inhaled in order to cause an infection.The signs of active TB disease, such as a cough, fever, night sweats, or weight loss, may not become apparent in a person for several months. This can cause delays in obtaining medical

attention and result in the spread of the infection to other people. Over the course of a year, individuals with active TB can infect 5–15 more persons through intimate contact.
Without effective treatment, virtually all HIV-positive and 45% of HIV-negative TB patients will die.

Causative organism

Mycobacterium tuberculosis is a species of pathogenic bacteria in the family Mycobacteriaceae and the causative agent of tuberculosis. First discovered in 1882 by Robert Koch, M. tuberculosis has an unusual, waxy coating on its cell surface primarily due to the presence of mycolic acid. This coating makes the cells impervious to Gram staining, and as a result, M. tuberculosis can appear weakly Gram-positive. Acid-fast stains such as Ziehl–Neelsen, or fluorescent stains such as aura mine are used instead to identify M. tuberculosis with a microscope. The physiology of M. tuberculosis is highly aerobic and requires high levels of oxygen.

Mycobacterium Tuberculosis Microbiology

M. tuberculosis sensustricto, M. africanum, M. canetti, M. bovis, M. caprae, M. microti, M. pinnipedii, M. mungi, and at least 9 other members of the complex were discovered in 2019.Orygis, M. It is non-motile, depends on oxygen to grow, and whether it generates spores is up for debate. Every 18 to 24 hours, M. tuberculosis divides. When compared to other bacteria, which typically measure their division times in minutes (Escherichia coli may divide around every 20 minutes), this is incredibly slow. It is a tiny bacillus that can tolerate ineffective disinfectants and endure for weeks in a dry environment. Its unique cell wall, which is abundant in lipids like mycolic acid, is probably what gives it resilience to desiccation andis a key virulence factor.

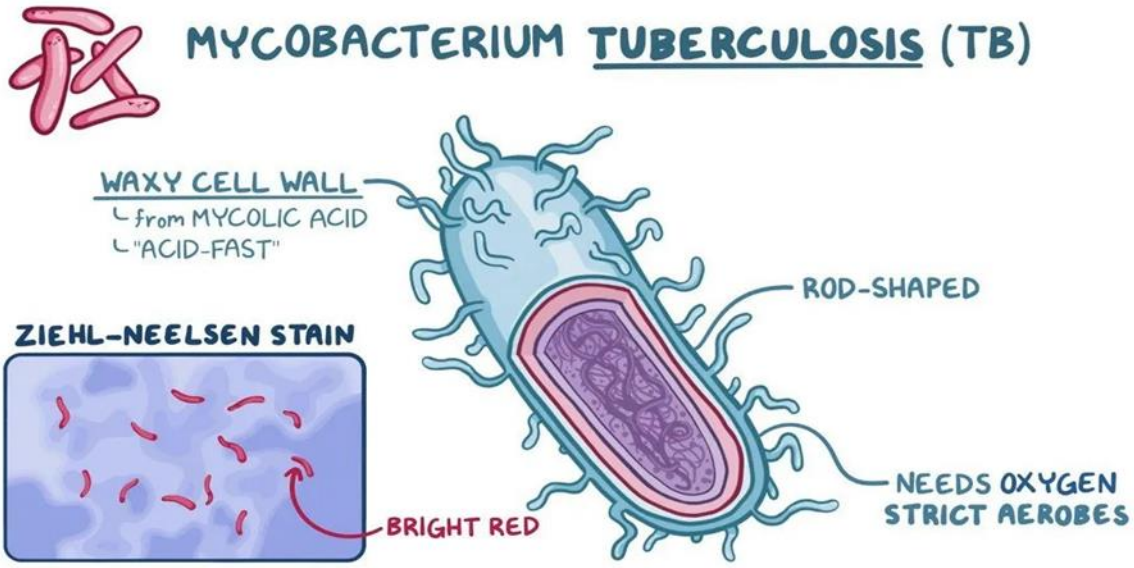

Fig 1.1: Mycobacterium Tuberculosis

2.2 Tuberculosis Pathogenesis

Infection happens when tubercle bacilli-containing droplet nuclei are inhaled and make their way to the lungs' alveoli. Alveolar macrophages consume these tubercle bacilli; the majority of these bacilli are killed or inhibited. When the macrophages die, a tiny portion may proliferate intracellularly and are expelled. If these bacilli are alive, they may move via lymphatic pathways or the bloodstream to more distant tissues and organs, such as the regional lymph nodes, apex of the lung, kidneys, brain,and bone—regions of the body where TB illness is most prone to occur. The immune system is prepared for a widespread reaction by this process of dissemination. This article provides more information on the pathogenesis of latent tuberculosis infection (LTBI) and TB illness.

Types of Tuberculosis

Pulmonary Tuberculosis: Fever is the most prevalent sign of lung tuberculosis Pleural Tuberculosis
Tuberculosis of the skeleton
Tuberculosis of the brain
Tuberculosis of the bladder and kidneys
Tuberculosis of the joints
Tuberculosis of the gastrointestinal tract
Tuberculosis of the miliary kind.

Symptoms of Tuberculosis

• **Latent TB**. Although humans have a TB infection, the bacteria are dormant and do not manifest any symptoms. It's not communicable to have latent TB, commonly known as dormant TB or TB infection. Treatment is crucial because latent TB might develop into active TB.

• **Active TB**. This illness, which is also known as TB disease, makes people ill and can typically spread to others. It can occur weeks or years after infection with the TB bacteria.

Signs and symptoms of active TB include:

• Coughing for three or more weeks • Coughing up blood or mucus • Chest pain, or pain with breathing or coughing • Unintentional weight loss• Fatigue • Fever • Night sweats • Chills • Loss of appetite

Causes of Tuberculosis

Microdroplets emitted into the air by germs that cause tuberculosis allow it to spread from one person to another. The active, untreated form of tuberculosis can cause this when a person coughs, speaks, sneezes, spits, laughs, or sings.

Having diabetes, end-stage kidney illness, and some malignancies are risk factors that enhance your likelihood of catching the bacteria that causes TB disease.an HIV diagnosis or another condition that compromises the immune system; malnutrition; prolonged use of tobacco or alcohol; People who use drugs that impair the immune system run the chance of contracting active TB illness. These include drugs that lessen the chance of organ rejection.

The following prescription drugs also enhance your risk of developing active TB:

- Cancer
- Rheumatoid
- Coaching
- Psoriasis
- Lumps

Classification of anti- tuberculosis drug

First line drug

Isoniazid
Rifampin
Pyrazinamide
Ethambutol
Streptomycin

Second line drugs

Fluoroquinolones

Oflaxacin
Levofloxacin
Moxifloxacin
Ciprofloxacin

Other oral drugs

Ethionamide
Prothionamide
Cycloserine
Para-amino- salacyclic acid (PAS)
Rifabutin

Injectable drugs

Kanamycin
Amikacin
Capreomycin

Drug Group A

Levofloxacin

It is an antibacterial agent made artificially. It works by preventing the enzymes required to split bacterial DNA, which prevents cell division.

Process of Action

A member of the fluoroquinolone medication class, levofloxacin is a bactericidal antibiotic that prevents bacteria from synthesising DNA. Levofloxacin encourages DNA strand breaks by preventing DNA-gyrase in organisms that are vulnerable to it from relaxing supercoiled DNA.

Levofloxacin's side effects

Levafloxacinare typically well tolerated. Nausea, vomiting, diarrhoea, difficulty sleeping, dizziness, and sensitivity to light are occasionally reported adverse effects. Peripheral neuropathy and tendon rupture are rare side effects.Levofloxacin's safety during pregnancy and breast-feeding is unknown. Levofloxacin should not be used during pregnancy or while nursing due to the possibility of major adverse effects, notably damage to cartilage. Only if benefits exceed risks should pregnant women use fluoroquinolones.

Moxifloxacin

Moxifloxacin, an 8-methoxy-fluoroquinolone, has a strong safety record and has proven to be an effective fluoroquinolone for the treatment of a variety of diseases, including community-acquired pneumonia.

Mechanism of action

A versatile antibiotic, moxifloxacin is effective against both Gram-positive and Gram-negative bacteria. It works by preventing the type II topoisomerase DNA gyrase and topoisomerase IV enzymes from separating bacterial DNA, which prevents cell division.

ISONIAZID

Isoniazid is an antibiotic used to treat and prevent active and latent tuberculosis (TB) (a serious infection caused by bacteria that affects the lungs and in certain cases other parts of the body). It functions by eradicating the tuberculosis-causing germs.

Mechanism of action

A prodrug called isoniazid prevents the mycobacterial cell wall from forming. The bacterial catalase-peroxidase enzyme KatG from Mycobacterium TB is required for the activation of isoniazid. The nicotinoyl-NAD adduct is created when the isonicotinic acyl radical spontaneously links with NADH as a result of KatG catalysing its production. This complex blocks the natural enoyl-AcpM substrate and the activity of fatty acid synthase by strongly binding to the enoyl-acyl carrier protein reductase InhA. Mycolic acids, essential building blocks of the mycobacterial cell wall, are prevented from being produced by this process. Nitric oxide, which has also been shown to be significant in the action of another antimycobacterial prodrug pretomanid, is one of the radicals created when KatG activates isoniazid.

Side Effects

Peripheral neuropathy can occur in as many as 20% of isoniazid users at dosages of 6 mg/kg daily or higher. Nausea and vomiting are examples of gastrointestinal responses. Insufficient production of red blood cells, platelets, or white blood cells by the bone marrow can also result in aplastic anaemia, thrombocytopenia, and agranulocytosis. The symptoms of hypersensitivity responses, which are also frequent, include fever and a maculopapular rash. Gynecomastia could happen.

10% to 20% of persons receiving INH experience asymptomatic elevations in serum liver enzyme levels, and even when medication is continued, liver enzyme levels typically revert to normal. Isoniazid has a boxed warning for severe and occasionally deadly hepatitis, which is age-dependent and occurs in people between the ages of 21 and 35 at a rate of 0.3%.

GROUP B Drugs

Amikacin

It is injected intramuscularly five times a week at a dose of 15 mg/kg once daily. The 0.5-g vial's contents are combined with 100 ml of sterile diluent (i.e., normal saline, 5% dextrose in water) to create the solution for intravenous use.

Mechanism of action

Amikacin's main mode of action is the same as that of all aminoglycosides. It attaches to bacterial 30S ribosomal subunits and disrupts tRNA acceptor sites and mRNA binding, which prevents bacterial growth.

Capreomycin

This particular antibiotic is used in conjunction with other antibiotics to treat tuberculosis. It is a second-line therapy used specifically for active drug-resistant tuberculosis. It is administered via injection into a muscle or vein.

Method of action

Although the precise mechanism of action of capreomycin is unknown, it is believed to suppress protein synthesis by interacting with the 70S ribosomal subunit. Additionally, the bacterial cell components that capreomycin binds to cause the creation of aberrant proteins. The existence of the bacterium depends on these proteins.

Kanamycin

Additionally, it is used to treat multi-drug resistant TB. Kanamycin, developed in 1957, is one of five medications often used in a treatment regimen to treat MDR TB. It belongs to a class of medications known as injectables.

Mechanism of action

An aminoglycoside antibiotic called kanamycin is used to treat various bacterial infections. By attaching to the bacterial 30S ribosomal subunit, kanamycin prevents the bacterium from synthesising proteins necessary for growth by causing mRNA to be misread.

Pyrazinamide

A drug is used to cure tuberculosis with it. It is frequently used with rifampicin, isoniazid, and either streptomycin or ethambutol to treat active tuberculosis. Generally speaking, it is not advised for the treatment of latent tuberculosis. It is ingested orally.

Nausea, a decrease in appetite, soreness in the muscles and joints, and rash are typical adverse effects. Gout, liver damage, and UV sensitivity are more severe side effects. In people with severe liver illness or porphyria, it is not advised. Although it is not certain if use is safe during pregnancy, it is probably safe when nursing. The class of drugs known as anti-mycobacterials includes pyrazinamide. It's not totally obvious how it operates.

Although pyrazinamide was created in 1936, it wasn't until 1972 that it was widely used.It is listed as one of the essential medications by the World Health Organization. Generic versions of pyrazinamide are readily accessible.

Mechanism of action

The bactericidal antibiotic pyrazinamide is chemically synthesised. The TB bacteria need to produce energy in order to survive, therefore it changes a particular enzyme into an active form that prevents the creation of fatty acids. This damages the cell membrane.

Market Survey of Anti-tubercular Drugs in Uttarakhand

AnoopDimri, TB officer examined systematic monitoring of cases, the health department has started collecting data on the number of cases and the medicines sold by private practitioners.

“TB has also been declared a notifiable diseases, so all practitioners are now duty bound to inform us about any new case.

It takes proper dose atleast 6 to 8 months to cure TB but if a patient gets infected with Multi-Drug Resistance Tuberculosis (MDRT), the process extended to 24 to 28 months of Directly Observed Treatment with short course chemotherapy (DOTS) and other medication.

XDR is the extreme stage, and 3 Uttarakhand patient have been affected by TB.

Work on TB prevention and treatment in the states is undertaken in coordination with the youth and welfare department, the integrated child development services (ICDS) women department ONGC and school education to spread and sanitised people.

Based on the nature of anti- microbial to the disease different treatment regimen are offered through the program. New Cases and those which exhibit no resistance are offered a six month, short course of the four first line drugs; Isoniazid-H, Rifampicin-R, Pyrazinamide –Z, and Ethambutol -E.

CONCLUSION

After the market survey of tuberculosis and anti-tubecular drugs, we found that most of the people are suffering from lungs tuberculosis. 58% of men are affected from tuberculosis, 36% of women are affected from tuberculosis and 6% of children are affected from tuberculosis. Isoniazid-H, Rifampicin-R, Pyrazinamide –Z, and Ethambutol –E are most useful medicines in the treatment of tuberculosis. People suffering from multidrug resistance tuberculosis (MDR-TB) have to undergo with the long term duration of 4-6 month to 24-28 month. This resistance works in against of Isoniazid and Rifampin. Malnutrition, high tobacco consumption and poor ventilation in buildings, coupled with low socio-economic status leads to tuberculosis. People who are unable to complete the tuberculosis medication due to some reason, pursue more chances of drug resistance. As we know that, tuberculosis is a communicable disease so the person in the contact with person who is suffering from tuberculosis may pursue tuberculosis due to improper sensitisation, poor hygiene. Now we conclude that, most of the people are not aware of tuberculosis, because of which tuberculosis is spreading a lot in India and tuberculosis is the most spreadable disease after COVID-19.

REFERENCES

1. Goel K., Kondagunta N, *et.al*. "Reasons for patient delays and health system delays for tuberculosis in South India". *Indian Journal of Community Health*, 23(2); 87-89.
2. Storla DG, Yimer S, *et.al*. 2008 "A systematic review of delay in the diagnosis and treatment of tuberculosis". *BMC Public Health*; 1-9.
3. Charles N, Thomas B, *et.al*. 2010 "Care seeking behaviour of chest symptomatic: A community based study done in South India after the implementation of the RNTCP", *Tuberculosis Research Center, Indian Council of Medical Research, Chennai, India*, 1-6.
4. Natesan M, Chauhan RC, *et.al*. 2015 "Patient and health system delay among new pulmonary tuberculosis patients diagnosed at medical college hospitals in Puducherry, India". *Int J Res Med Sci*, 188-193.
5. Kulkarni PY, Kulkarni AD, *et,al.* 2013 "Treatment seeking behaviour and related delays by pulmonary tuberculosis patients in E-ward of Mumbai Municipal Corporation", *India. Int J Med Public Health*, 286-292.
6. Shamim H, Vidyasagar SS, *et,al.* 2015 "Health care seeking behaviour of cough symptomatic (pulmonary tuberculosis suspects) attending medicine outpatient department of a tertiary care hospital of Jharkhand". *Int J InterdiscipMultidiscip Stud.* 42-49.
7. Ananthakrishnan R, Jeyaraju AR, *et.al.* 2012 "Care seeking behavior of the TB patients who were registered in an urban government tuberculosis control*" tuberculosis research centre in Chennai, Tamil Nadu,India. J ClinDiagn Res*, 990-993.
8. Karanjekar VD, Gujarathi VV.2014 "Socio demographic factors associated with health seeking behaviour of chest symptomatic in urban slums of Aurangabad city, India". *Int J Appl Basic Med Res*, 173-179.
9. Kaur M, Sodhi SK, *et.al.* 2013 "Gender differences in health care seeking behaviour of tuberculosis patients in Chandigarh". *Indian J Tuberi*, 217-222.
10. Thakur R, Murhekar M.2010 "Delay in diagnosis and treatment among TB patients registered under RNTCP Mandi, Himachal Pradesh, India". *Indian J Tuberc*, 37-45.
11. Barry, C. E. 3rd *et.al.* 2009 "The spectrum of latent tuberculosis: rethinking the biology and intervention strategies". *Nat. Rev. Microbiol*. 845– 855.
12. Marais, B. J., *et.al*.2006 "Childhood pulmonary tuberculosis: old wisdom and new challenges". *Am.J. Respir. Crit. Care Med.* 1078- 1090.
13. Swaminathan.S. , Rekha, B.2010 "Pediatric tuberculosis: global overview and challenges". *Clin. Infect. Dis.* 184–194.
14. Wood R, Racow K, Bekker LG, *et.al*.2012 "Indoor social networks in a South African township: potential contribution of location to tuberculosis transmission". *PLoS One* 392-402.
15. Andrews JR, Morrow C, *et.al* .2013 "Modelling the role of public transportation in sustaining tuberculosis transmission in South Africa". *Am J Epidemiol* 556 – 561.
16. Roetzer A, Diel R, Kohl TA, *et.al*.2013 "Whole genome sequencing versus traditional genotyping for investigation of a Mycobacterium tuberculosis outbreak: a longitudinal molecular epidemiological study*". PLoS Med*, 1-12.
17. Ajbani, K. K, Rodrigues, C, *et.al*. 2012 "Totally drug-resistant tuberculosis in India". *Clin. Infect. Dis*. 579–581.
18.Jenkins,H.E. et al. 2013 "Assessing spatial heterogeneity of multidrug-resistant tuberculosis in a high-burden country. *Eur. Respir. J*. 1291–1301.
19.Zelner, J. L. *et al*. 2016 "Identifying hotspots of multidrug resistant tuberculosis transmission using spatial and molecular genetic data. *J. Infect. Dis*. 287–294.
20.Fofana, M. O. Dowdy, D. W, *et al*. 2015 "Burden of transmitted multidrug resistance in epidemics of tuberculosis: a transmission modelling analysis*". Lancet Respir. Med.* 963–972.
21. DR. E. , SaraceniV,*et al*.2012 "Heterogeneity in tuberculosis transmission and the role of geographic hotspots in propagating epidemics". *Proc. Natl Acad. Sci. USA*, 9557–9562.
22.Dye, C.2006 "Global epidemiology of tuberculosis". *Lancet* 938–940.
23.*The American Society of Health-System Pharmacists.* Archieved from the original on 20 December 2016. Retrieved 8 December 2016.
24. Steichen, O.; Martinez-Almoyna, L.; De Broucker, T. (April 2006). "Isoniazid induced neuropathy: consider prevention" (PDF). *Revue des Maladies Respiratoires*. 23 (2 Pt 1): 157–160.
25.Timmins, G.S.; Master, S; Rusnak, F.; Deretic, V. (August 2004). "Nitric oxide generated from isoniazid activation by KatG: source of nitric oxide and activity against Mycobacterium tb. *Antimicrobial Agents and Chemotherapy*. 48 (8): 3006–3009.