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PULMONARY MYCOBACTERIUM TUBERCULOSIS: REVIEW ARTICLE

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Abstract:

Pulmonary tuberculosis (PTB) is a contagious diseases caused by bacteria called (Mycobacterium tuberculosis) that usually effect the lungs and it can spread to other parts of the body. TB can cause symptoms such as coughing, chest pain, coughing up blood or phlegm, fever, night sweats, fatigue, and weight loss. TB can be diagnosed with several tests, including a X-ray for chest and a sputum test. Eliminate disease involves taking antibiotics for at least six months. TB can be prevented with a vaccine called the Bacillus Calmette-Guérin (BCG) vaccine and by avoiding contact with people who have active TB. Early diagnosis and medication of Pulmonary tuberculosis are important to prevent the disease.

Introduction:

Mycobacterium tuberculosis is a bacterial caused Pulmonary tuberculosis (PTB) by inhale small drop from the coughs or sneezes from infection person. The bacillus is the cause of tuberculosis, and without it, cannot occur tuberculosis. Pulmonary tuberculosis mainly affects the lungs. TB is a potentially condition, and can be treated it with the right antibiotics. ^[1] People are now vaccinated with BCG so they can be prevented from being infected with this disease. ^[2] *M. tuberculosis*, is acid-fast bacillus, not –sporulation, non-motile, elective, H2O2 –negative, inside cell microorganism ^[3]. The organism has contained some specific characteristics differ from other bacteria for ex. found lipid in the cell wall of bacteria containing mycolic acid, cord factor, and Wax-D. The elevated waxy in the cell wall consider virulence factors for:

- renitent to many drugs.
- Hardness smearing with traditional dyes
- The capability of endurance harsh circumstances such as acid or alkaline, minimum O2 level & occurring within a cell (inside macrophages)

The acid-fast stain is one of the most common stain for diagnosing tuberculosis. A positive result will kept the pink color of carbol fuchsin dye, called this, acid-fast bacilli (AAFB). ^[3]



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

The Cause of Tuberculosis:

Mycobacterium tuberculosis (Mtb)is bacteria caused Tuberculosis and consider contagious disease . According to the World Health Organization (WHO), (Mtb) is consider one of the leading causes of death worldwide. With nearly 8 million new cases each year and more than 1 million deaths per year, tuberculosis is still a public health problem. Despite the decrease in incidence, morbidity and mortality remain important, partially due to co-infection with the human immunodeficiency virus and the emergence of resistant bacilli.^[4] Mtb invades through the airway, subverts host immunity, establishes its survival niche, and ultimately escapes in the setting of active disease to initiate another round of infection in a naive host. [5-6]. The introduction of unexplained short courses of chemotherapy, decreased attention of physicians to pathogenesis treatments, and failure to adhere to the screening standard during transition to other follow-up of clinically treated patients increased the risk of early tuberculosis recurrence. In future years, there may be a further rise in the number of late recurrence cases in the general population of the Russian Federation as preventive measures have deteriorated among individuals treated for TB after referral to the public health care system. Persons who have experienced tuberculosis and were struck off the register in a tuberculosis dispensary more than 5 years ago make up a late recurrence risk group. [7] In 1882, Robert Koch showed that the bacillus was the cause of tuberculosis. This scientific breakthrough led to a revolution in pathology that had enormous implications for the control of infectious diseases, the repercussions of which are still being felt to this day. [8]

Pathophysiology:

Tuberculosis lung infection is a multisystem disease .The common way for infection spreads out of breathing in of effected droplets . The body's capability to efficaciously reduce the infectious inoculum depends on the patients' immunity , genetic factors, and primary or secondary exposure to the bacteria . TB has various virulence factors that make it harsh for phagocytosis . Virulence factors include a rising content of mycolic acid in the cell wall of bacteria and found other substances in the cell wall ex. cord factor right away hurt alveolar macrophages. Many research have shown that Mycobacterium tuberculosis inhibits effective macrophage forming , thus prevention or tuning the removal of the bacteria . The early entry of the *Mycobacterium* inside the body leads to Clinical signs recognize as primary tuberculosis . primary TB is stationed to the midst part of the lungs, and this is recognize as the Ghon focus of primary TB . most TB patients for Ghon focus enters a state of latency. This condition is recognize as latent tuberculosis. Latent tuberculosis can be restore activity for immunosuppression host. ^[9-10]

Type-IV Hypersensitivity and Caseating Granuloma

Tuberculosis is a vintage ex. a late-onset type IV hypersensitivity reaction.

late hypersensitivity reaction: By activation immune cells (T helper lymphocytes, CD4+ cells), Mycobacterium tuberculosis stimalution the induction and energetic of tissue macrophages. This procedure is advanced and sustained by the make of cytokines, mostly interferon-gamma.



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

macrophages is under going (2) major alteration firstly forming of giant cells and epithelioid cells. This change used for Improve phagocytosis. Collection of Giant cell a round Mycobacterium particle and lymphocytes is recognize as a granuloma.

Epithelioid cells ability for cytokine synthesis.

The granuloma in tuberculosis has been refer as caseous or cheesy. This refers to the high level of mycolic acid content in the bacteria cell wall, Because high level of wax caseous or caseating ,necrosis was used to refer to granuloma necrosis caused by Mycobacterium tuberculosis. ^[11]

Signs and Symptoms:

Symptoms of pulmonary TB infection depend on bacteria are growing inside the body. TB bacteria usually grow in the lungs (pulmonary TB). Pulmonary TB disease may cause a bad persistent cough that lasts 3 weeks or longer, pain in the chest, and coughing accompanied with blood or sputum (phlegm) from deep inside the lungs. Other symptoms of disease are:

- weakness or fatigue.
- chills.
- fever.
- weight loss
- no appetite
- sweating at night.^[12]

People Who have Latent TB Infection:

- Have no symptoms.
- Don't feel sick.
- You can't spread TB bacteria to others.
- Usually have a positive TB skin test reaction or positive TB blood test.
- They may develop TB disease if they do not receive treatment for latent TB infection.^[13]

Epidemiology

overall of 1.6 million people died from tuberculosis in 2021. Worldwide, Tuberculosis is the third major cause of death and the second major cause of death after COVID-19. In 2021, an rate 10.6 million people will fall ill with tuberculosis worldwide. Six million men , 3.4 million women, and 1.2 million children . Tuberculosis is existent in all countries and all age groups, but it is curable and able to be prevented or avoided. TB can spread when a person with active TB disease releases germs into the air through coughing, sneezing, talking, singing, or even laughing. An active lung infection is contagious. Most people who inhale TB bacteria can get rid of the bacteria and prevent it from growing and these bacteria become inactive in these individuals, causing a latent TB infection. Even though the bacteria are inactive, they are still alive in the body and can become active at a later time. Some people can have a latent TB infection for life without becoming active and developing TB. However, TB disease can become active if your immune system is weakened and cannot stop the growth of the bacteria. This



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

occurs when a latent TB infection becomes active. Many researchers are working on treatments to prevent this from occurring. ^[14-15]

There was high prevalence of *Mtb* in Baghdad Governorate and most infections were in Al-Rusafa side and there was no significant difference in infections between seasons. ^[16]

The incidence of TB in Erbil city remarkably increased in the years 2015 (20.3 per 100,000 inhabitants) and 2016 (21.7 per 100,000 inhabitants). Such an increase might be related to the massive population displacement from Mosul and the surrounding areas to Erbil because of the ISIS related confict in 2014. Such displacement resulted in having TB patients from Mosul who suffered from a lack of access to health care. There were also a large number of displaced and refugee people coming from remote areas and hard to reach locations. ^[17]

Five major factors influence TB epidemiology: [18]

1. Socio-economic state : The main factors leading to the eliminate of TB cases are the improvement of social and housing state . Most cases occur in low-income countries. In industrialized countries

2. Tuberculosis medication : starting effective medication for a patient early in the course of TB before it infects multiple people is the most effective preventive measure against TB. Once effective TB treatment is initiated, there is a rapid decline in transmission. Since the introduction of tuberculosis treatment, the risk of contracting tuberculosis has decreased by about 10% per year in industrialized countries.

3. HIV infection: HIV infection is a major risk factor for progression to active tuberculosis and has a significant impact on tuberculosis . While the lifetime risk of developing active TB in the general population is 5 to 10% after infection with TB, this risk is about 10% per year in patients infected with HIV and TB.

4. Diabetes : The risk of tuberculosis is higher among diabetics than among non-diabetics. It is estimated that diabetes contributes to 15% of tuberculosis cases worldwide.

5. BCG Vaccine : If given at birth, it is very effective against severe forms of tuberculosis (miliary and meningitis) in children.

People at High Risk for Exposure to or Infection with Mycobacterium tuberculosis include: [19]

• Contact with people infected or suspected of having tuberculosis.

• People who live or have lived in high-risk effect places

• Population locally defined as having an increased incidence of tuberculosis, or people who abuse drugs or alcohol. People at risk of contracting TB include:

- People living with HIV
- Children over 5 years old
- People infected with tuberculosis recently (within the past two years).
- People with a history of untreated or inadequately treated tuberculosis
- Smokers of cigarettes or alcohol.



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

Diagnosis:

Different types of TB have different ways of diagnosis:-

1- Pulmonary tuberculosis:

Diagnosing pulmonary tuberculosis — tuberculosis that affects the lungs — can be difficult . X-ray for chest to look changes appearance of lungs and that suggestive of TB. Often samples of sputum are taken and checked it for the presence of TB bacteria . These tests are very important to determine infection

2- Extrapulmonary tuberculosis:

Many tests can be used to confirm of extrapulmonary TB, which is tuberculosis outside the lungs. These tests include:

MRI or ultrasound scan of the affected body part. examined urine , blood tests and a biopsy is taken - a small swab of tissue or fluid is taken from the infected region .

A lumbar puncture, a small sample of cerebrospinal fluid (CSF) is possessed from patients. The sample can be checked to see TB has infected the brain and spinal cord (central Nervous system). ^[20-21]

Management:

There is sparse evidence on the effectiveness and safety of using anti-TB drugs to prevent active TB among adult and childhood contacts of multi-drug resistance (MDR-TB) cases. Furthermore, determination of the drug susceptibility profile for drugs to be used as preventive treatment for MDR contacts poses both technical and logistic challenges and may lead to drug-related harms, which would necessitate additional cost for close monitoring which has resource implications. It was concluded that the available evidence showed no significant association between anti-TB drug resistance and the use of isoniazid and/or rifamycins for LTBI. However, the panel emphasized the importance of establishing national TB drug resistance surveillance systems in countries implementing systematic testing and treatment for LTBI.^[22-23]

Treatment

Medication of diseases :

Medication of TB need a Mixing more than one medicine. Multiple drugs is constantly indicated for diseases and mono-drug don't be used for tuberculosis because dose not work .^[24]

Drugs of choice for treated TB:

1st –line medication regimen , set 1

- ≻ Isoniazid .
- Rifampicin.
- ≻ Rifabutin .
- Rifapentine .
- Pyrazinamide .
- Ethambutol.



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

Isoniazid and Rifampicin ,After that, four types of medicines are used involve Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide) for two months or 6 months. Vitamin B6 is constantly offered with Isoniazid to stop neural harm (neuropathies). ^[25]

2st –line medication regimen % 2st , set 2

- Amikacin
- > Kanamycin
- > Streptomycin

2st -line medication regimen, set three,

- Fluoroquinolones.
- > Levofloxacin.
- > Ofloxacin.
- Gatifloxacin

2st -line medication regimen , set four

- Para-aminosalicylic acid
- > Cycloserine
- ➤ Terizidone
- ➢ Ethionamide
- Prothionamide
- > Thioacetazone
- ➢ Linezolid

3rd -line medication regimen, set 5

- Clofazimine
- ➤ Linezolid
- Amoxicillin/clavulanic acid
- ➢ Imipenem/cilastatin
- Clarithromycin

MDR-TB, XDR-TB

Multidrug- renitent tuberculosis had become more widespread. collection of $1^{\rm st}$ -line and $2^{\rm nd}$ -line drugs in high doses is used to treat this condition.

MDR-TB, XDR-TB

Multidrug- renitent tuberculosis had become more widespread.

A collection of 1^{st} -line and 2^{nd} -line drugs in high doses is used to treat this condition. ^[26]

Multi-Drug renitent Tuberculosis (MDR-TB) and Extremely Multi-Drug renitent Tuberculosis (XDR-TB)

MDR-TB

• *Mycobacterium* strain have renitent to the classic anti-tuberculosis drugs. renitent to multiplied anti-tuberculosis drugs content at least the 2 anti-TB drugs, Rifampicin or Isoniazid, is wanted to make a diagnosis of MDR-TB.



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75% of MDR-TB is considered primary MDR-TB, caused by infection with MDR-TB pathogens. The remaining 25% are wanted and occur when a patient develops renitent to medication for TB, because of several factors such as Inappropriate use of the treatment; not enough dose ; imperfect therapy is the number one cause of acquired MDR-TB.^[27]

XDR-T.B

- This type is a more severe from MDR-TB. Diagnosis wanted renitent to at least 4 antituberculous drugs including renitent to Rifampicin, Isoniazid, and renitent to any 2 of the new anti-TB drugs . The new drugs for XDR-TB are the fluoroquinolones (Levofloxacin and moxifloxacin) and the injectable second-line aminoglycosides, Kanamycin, Capreomycin, and amikacin.
- Action for XDR-TB is identical to the action of MDR-TB.
- XDR -TB is an rare

Differential Diagnosis

Tuberculosis is a major tradition and must be taken into account in the differential diagnosis of many systemic disorders. ^[28]

- Pneumonia
- Malignancy
- Non-tuberculous mycobacterium
- Fungal infection
- Histoplasmosis
- Sarcoidosis

Management of toxic and harmful effects:

Most common side effects associated with anti-TB drugs : [29]

1) Isoniazid- showing no symptoms. rise of aminotransferases, clinical hepatitis, hypersensitivity.

2) Rifampin- Pruritis, nausea & vomiting, flulike symptoms, hepatotoxicity, orange discoloration of body fluid.

- 3) Rifabutin- Neutropenia, uveitis, polyarthralgias, hepatotoxicity.
- 4) Rifapentine- Similar to rifampin
- 5) Pyrazinamide- Hepatotoxicity, nausea & vomiting, polyarthralgias, acute gouty arthritis.

One of the most important aspects of tuberculosis treatment is follow-up and observation for these side effects. when observe side effects should be close monitoring or stop the drug .

Prognosis: [30]

- The majority of patients diagnosed with Tuberculosis have a perfect result. This is mainly due to the efficacious therapy, Without treatment, the death rate from tuberculosis is more than 50%.
- The following group of patients is more likely to have a worse result or death after affected TB:
- elderly, infants, and young children



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

- Delay in taking treatment
- Respiratory settlement requiring mechanical ventilation
- Immunosuppression

Complications : [31]

Complications are repeatedly seen in effect person . Some cases related to the tuberculosis are:

- Extensive lung destruction
- Damage to cervical sympathetic ganglia leading to Horner's syndrome.
- Acute respiratory distress syndrome
- Milliary spread (disseminated tuberculosis)including TB meningitis.
- Empyema
- Pneumothorax
- Systemic amyloidosis

Conclusion:

TB is a major public health concern worldwide and remains the world's second-most common cause of death from infectious disease after HIV/AIDS. With the emergence of drug-resistant strains, clinicians must understand the pathology, clinical manifestations, diagnosis, and management of this disease. Early identification and treatment reduce transmission and prevent increases in patient morbidity and mortality.

Reference:

1.Ali ZA, Al-Obaidi MJ, Sameer FO, *et al.*: Epidemiological profile of tuberculosis in Iraq during 2011–2018. *Indian J. Tuberc.* 2022; 69(1): 27–34.

2. Hadi Jebur Suhail,Saad Mashkoor Waleed, Yasmeen Ali Hussien and Salim Fayez KadhimTuberculosis: A Multi-Drug Risk Study in Al-Diwaniyah Governorate, Iraq. Sys Rev Pharm 2020; 11(2): 165 169.

3.Mohammed SH, Ahmed MM, Al-Mousawi AM, et al.: Seasonal behavior and forecasting trends of tuberculosis incidence in Holy Kerbala, Iraq. Int. J. Mycobacteriol. 2018; 7(4): 361–367.

4-Mjid M, Cherif J, Ben Salah N, Toujani S, Ouahchi Y, Zakhama H, Louzir B, Mehiri-Ben Rhouma N, Beji M. Épidémiologie de la tuberculose [Epidemiology of tuberculosis]. Rev Pneumol Clin. 2015;71(2-3): 67-72.

5-Taif Saad Jasim , Amer Hayat Khan and Nada Khazal K Hindi.Prevalence of tuberculosis infection and treatment outcome in Babylon Province of Iraq: A retrospective study. Medical Journal of Babylon.2023; 20:194-200.

6.Rahlwes KC, Dias BRS, Campos PC, Alvarez-Arguedas S, Shiloh MU. Pathogenicity and virulence of Mycobacterium tuberculosis. Virulence. 2023;14(1):2150449.

7.Stehbens WE. On the "cause" of tuberculosis. Pathology. 1987;19(2):115-9.



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

8. Zumla A, Raviglione M, Hafner R, Fordham von Ryen. Current concepts: tuberculosis. N Engl J Med. 2013;368:745–755.

9. Knechel NA. Tuberculosis: pathophysiology, clinical features, and diagnosis. Crit Care Nurse. 2009;29:34–43.

10.Singh, R.; Dwivedi, S. P.; Gaharwar, U. S.;Meena, R.; Rajamani, P. and Prasad, T. Recent updates on drug resistance in Mycobacterium tuberculosis.

Journal of Applied Microbiology.2020; 128:1547–1567.

11. Ahmed MM. Tuberculosis situation in Iraq: a puzzle of estimates. Int J Mycobacteriol. 2013;2(4):248–249.

12. Frieden TR, Sterling TR, Munsiff SS, et al. Tuberculosis. Lancet. 2003;362:887–899.

13. Hargreaves JR, Boccia D, Evans CA, Adato M, Petticrew M, Porter JD. The social determinants of tuberculosis: from evidence to action. Am J Public Health. 2011;101:654–662.

14.Abdulla NY, Aljanaby IJA, Hasan TH, et al.: Assessment of β-lactams and Carbapenems Antimicrobials Resistance in Klebsiella Oxytoca Isolated from Patients with Urinary Tract Infections in Najaf, Iraq. Arch. Razi Inst. 2022; 77: 669–673.

15. Rosli NM, Azhar Shah S, Mahmood M. Geographical Information System (GIS) application in tuberculosis spatial clustering studies: a systematic review. Malays J Public Health Med. 2018;18:70–80.

16.Salah Tofk, Jalal Balaky· Arthur Saniotis, Ahang Hasan Mawlood, Ali M. Hussein, Nazar P. Shabila. Incidence and geographical distribution of tuberculosis disease in Erbil city, Iraq .Brazilian Journal of Microbiology. 2022;53:519–523.

17.Al-Saeedi, M. and Al-Hajoj, S. . Diversity and evolution of drug resistance mechanisms in Mycobacterium tuberculosis. Infection and Drug Resistance.2017; 10: 333–342.

18.Zainab A. Ali, Ahmed A. Mankhi, Ali H. Ad'hiah.Interleukin-37 gene polymorphism and susceptibility to pulmonary tuberculosis among Iraqi patients. Indian Journal of Tuberculosis.2022; 69:191-200.

19. Hussein N, Balatay AA, Almizori LA, Saifullah HH. A study of the prevalence of latent tuberculosis in household contacts of patients with active tuberculosis in Kurdistan Region of Iraq: a brief report. Int J Infect. 2019;6:e90402.

20. Mohammed SH, Ahmed MM, Mohammed ZH, Adeboye A. High risk disease mapping and spatial effect of pulmonary tuberculosis in Kerbala, Iraq. Biomed Biotechnol Res J. 2019;3:150–155.

21.Bushra J. Taqi Sanaa J. Kadhim. Estimation of miR-16 Gene Expression in Iraqi Tuberculosis Patients and Its Association with Response to Therapy. Iraqi Journal of Biotechnology. 2022; 21:522-528.

22.Zhai, W.; Wu, F.; Zhang, Y.; Fu, Y. and Liu, Z. The immune escape mechanisms of Mycobacterium tuberculosis. International Journal of Molecular Sciences.2019;20: 340.

23. Mustafa I, Najib B, Al TN. Association between life-style factors and pulmonary tuberculosis in Erbil. Zanco J Med Sci. 2018;15:6–11.



ISSN: 2776-1010 Volume 4, Issue 10, Oct. 2023

24.Drain, Paul K et al. "Incipient and Subclinical Tuberculosis: a Clinical Review of Early Stages and Progression of Infection." Clinical microbiology reviews .2018; 31,4 e00021-18.

25. World Health Organization. Global tuberculosis report 2018, https://apps.who.int/iris/handle/10665/274453.

26. Norbis L, Miotto P, Alagna R, Cirillo DM. Tuberculosis: lights and shadows in the current diagnostic landscape. New Microbiol. 2013;36:111–120.

27. Esmail H, Barry CE 3rd, Wilkinson RJ. Understanding latent tuberculosis: the key to improved diagnostic and novel treatment strategies. Drug Discov Today. 2012;17:514–521.

28.Getahun, Haileyesus et al. "Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries." The European respiratory journal .2015;46:1563-76. 29. Skachkova EI, Nechaeva OB, Aref'eva EV, Iasinetskaia NV. [Monitoring of tuberculosis recurrences: their causes and precipitating factors]. Probl Tuberk Bolezn Legk. 2008;8:16-9.

30. Barnes DS. Historical perspectives on the etiology of tuberculosis. Microbes and infection. 2000 ; 2:431-40.

31.Zainab A. Ali , Mohammed J. Al-Obaidi ,Fadhaa O. Sameer , Ahmed A. Mankhi , Khawla I. Misha'al , Iftikhar A. Jassim , Estabraq A. Taqi , Ali H. Ad'hiah.Epidemiological profile of tuberculosis in Iraq during 2011–2018 .Indian Journal of Tuberculosis.2022; 69: 27-34.

مقاله عن السل الرئوي الخلاصه: (Mycobacterium tuberculosis) السل الرئوي هو مرض معدي تسببه بكتيريا (Mycobacterium tuberculosis) أجزاء أخرى من الحسم. يمكن أن يسبب السل أعر اضًا مثل السعال و ألم الصدر و السعال المصحوب

و عادة ما تصيب الرئتين ويمكن أن تنتشر إلى أجزاء أخرى من الجسم. يمكن أن يسبب السل أعراضًا مثل السعال وألم الصدر والسعال المصحوب بالدم أو البلغم والحمى والتعرق الليلي والتعب وفقدان الوزن. يمكن تشخيص السل بعدة اختبارات ، بما في ذلك فحص الصدر بالأشعة السينية واختبار Bacillus البلغم. يتضمن القضاء على المرض تناول المضادات الحيوية لمدة ستة أشهر على الأقل. يمكن الوقاية من السل بلقاح يسمى لقاح وتجنب الاتصال بالأشخاص المصابين بالسل النشط. يعتبر التشخيص والعلاج المبكر لمرض السل الرئوي أمرًا (BCG) مهمًا للوقاية من المرض.

مفتاح المقاله هو :السل الرئوي