Readers Insight
Publisher of open access books and journals

PJMLS

Print ISSN: 2707-4471. Online ISSN: 2707-448X

Research Article | Pak-Euro Journal of Medical and Life Sciences
DOI: 10.31580/pjmls.v7i2.3038
Vol. 7 No. 2, 2024: pp. 338i-338q
www.readersinsight.net/pjmls
Revised: March 15, 2024 Accepted: March 18, 2024
Submission: January 09, 2024 Published Online: June 30, 2024

Copyright © All rights are reserved by Corresponding Author

PHYSIOLOGICAL AND BIOCHEMICAL ASPECTS OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS (EPTB) IN TEENAGERS IN BALOCHISTAN

Nawab Ud Din[1], Hina Ali Ahmed[2], Dur Khatoon Hayat[2], Abdul Hakeem[3], Pari Gul[4], Ayisha Khalid[5], Zia u Din[1], Tahir Hameed[1]*

[1]**Center for Advanced Studies in Vaccinology and Biotechnology (CASVAB),** University of Balochistan, Quetta, Pakistan

[2]**Department of Zoology,** Sardar Bahadur Khan Women University (SBKWU), Quetta, Pakistan

[3]**Deparment of Plant Pathology,** Lasbela University of Agriculture, Water and Marine Sciences (LUAWMS), Uthal, Pakistan

[4]**Institute of Biochemistry,** University of Balochistan, Quetta, Pakistan

[5]**Department of Pharmaceutical Chemistry,** Faculty of Pharmacy and Health Sciences, University of Balochistan, Quetta, Pakistan

***Corresponding Author:** Tahir Hameed. E. mail: tahirquetta@hotmail.com

Abstract

Background: *Tuberculosis (TB), caused by the Mycobacterium tuberculosis complex, remains a leading cause of global morbidity and mortality. While pulmonary tuberculosis (PTB) accounts for the majority of cases, extrapulmonary TB (EPTB) presents significant diagnostic challenges due to its heterogeneous clinical manifestations and the poor sensitivity of routine microbiological tests. This study aimed to examine the physiological and biochemical characteristics of active TB patients undergoing anti-tuberculosis therapy (ATT) in comparison to healthy controls, focusing on a teenage population in Balochistan, Pakistan.*

Methods: *This study enrolled 200 participants (100 confirmed TB patients and 100 age-matched healthy controls) from the Fatima Jinnah Chest and General TB Sanatorium Hospital and the Center of Advanced Studies in Vaccinology and Biotechnology (CASVAB), Quetta, between August 2021 and April 2023. Participants were stratified into three age groups (13, 14-16, and 17-19 years). Data on demographics, anthropometrics, complete blood count (CBC), liver function tests (LFTs), lipid profiles, and renal markers were collected and analyzed using SPSS version 22. Descriptive statistics, paired t-tests, and correlation analyses were employed, with a significance level set at $p < 0.05$.*

Results: *The study population was predominantly male (58%) and from the 17-19 years age group (62%). A significant proportion of patients had a normal-to-low body mass index (BMI) and belonged to the middle socioeconomic class. Hematological analysis revealed derangements, including leukocytosis (36%) and anemia (79% had low hemoglobin). Liver function tests showed generally normal bilirubin levels, but elevated alanine transaminase (SGPT/ALT) was observed in 26% of patients. Dyslipidemia was common, characterized by hypertriglyceridemia (16%) and low high-density lipoprotein (HDL) levels (63%). Comparative analysis between patients and controls revealed statistically significant differences in most CBC parameters, including hematocrit, mean corpuscular volume, and platelet counts ($p < 0.05$), while red blood cell and monocyte counts did not differ significantly.*

Conclusion: *This study highlights the critical importance of hematological, hepatic, and metabolic monitoring during ATT. While some hematological abnormalities improve with therapy, dyslipidemia may persist and requires concurrent management. These findings underscore the need for standardized protocols to mitigate treatment-related hepatotoxicity and justify further research into the metabolic consequences of TB, particularly in endemic regions like Pakistan*

Keywords: *Adolescents, Anti-Tuberculosis Therapy (ATT), Biochemistry, EPTB, Hematology, Tuberculosis*

INTRODUCTION

Tuberculosis (TB) is a historic and persistent social health issue in both developed and developing nations. It is a chronic infectious disease caused by the rod-shaped, non-sporing aerobic bacterium Mycobacterium tuberculosis. In 2019, an estimated 10.0 million people worldwide were infected with TB.

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The disease burden is highly heterogeneous, with significant prevalence in regions such as India (26%), Indonesia (8.5%), China (8.4%), and Pakistan (5.7%), according to the World Health Organization (WHO) (1, 2).

The primary mode of transmission for laryngeal or pulmonary TB is through ambient airborne droplets, known as droplet nuclei, which are produced when an infected individual sneezes, coughs, or speaks. These droplet nuclei contain bacilli that, when inhaled, adhere to the pulmonary alveoli (3, 4). The M. tuberculosis complex is the key etiologic agent, exerting a major impact on human mortality and morbidity globally (5).

TB is clinically classified into two major types: pulmonary TB (PTB) and extrapulmonary TB (EPTB) (6). EPTB can involve any organ and presents a wide range of clinical signs and symptoms, manifesting as laryngeal TB, cavitary TB, miliary TB, TB pleurisy, as well as infections of the lymph nodes, meninges, pericardium, peritoneum, and musculoskeletal, genitourinary, and other systems (7-9). Of the 7.5 million PTB cases reported globally, approximately 16% are estimated to be EPTB (10, 11).

The main clinical signs of PTB include fevers, a persistent cough lasting over two weeks, nocturnal diaphoresis, and unexplained weight loss. Diagnosis is often guided by these symptoms, and physical examination may reveal fever, tachycardia, and abnormal thoracic findings. EPTB presents more variably, with symptoms such as abdominal pain, markedly swollen lymph nodes, headache, confusion, and pain or loss of function in affected bones or joints (12, 13). Diagnosing EPTB is particularly challenging due to its varied symptomatology, the difficulty in obtaining representative samples from affected sites, and the pauci-bacillary nature of the disease, which limits the sensitivity of standard microbiological tests (14-16). Histopathological diagnosis relies on identifying granulomas, caseation, and acid-fast bacilli (AFB). However, a weakened host immune response can lead to reduced granulomatous reactions, and similar inflammation can be caused by non-tuberculous mycobacteria, fungi, or other infections, necessitating careful interpretation (17, 18).

In Pakistan, TB remains a significant public health challenge. Teenagers, in particular, represent a vulnerable subgroup due to a combination of biological, anatomical, physiological, and social factors. The motivation for this study stems from the current epidemiological issues related to TB among adolescents in the Balochistan region. This research aims to provide a detailed examination of the physiological and biochemical profiles of teenagers with active TB, comparing them with healthy controls, to improve clinical management and inform public health strategies.

MATERIALS AND METHODS

RESEARCH DESIGN AND SETTING

This study was conducted at the Fatima Jinnah Chest and General TB Sanatorium Hospital and the Center of Advanced Studies in Vaccinology and Biotechnology (CASVAB), Quetta, Balochistan, from August 2021 to April 2023. The study employed a comparative, cross-sectional design involving 200 subjects: 100 patients with confirmed active tuberculosis and 100 healthy controls. Written informed consent was obtained from all participants or their legal guardians. Ethical clearance was granted by the local ethics committee of CASVAB, Quetta, Pakistan.

DATA SAMPLING AND COLLECTION

Data were collected by professional paramedics and medical doctors using a pre-tested questionnaire. The questionnaire captured demographic information such as name, age, gender, residence, ethnicity, socioeconomic status, and family history. Participants were stratified into three age categories: 13 years, 14-16 years, and 17-19 years.

INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria for Patients: Patients were included if they were undergoing anti-tuberculosis treatment (ATT), had a sputum smear-positive result, and had a history of medication. Psychological and environmental stress was documented to be within acceptable limits. Other conditions for inclusion were

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

normal chest computed tomography (CT) findings, a confirmed GeneXpert report, and the absence of any chronic disease. Individuals were excluded from the tuberculosis cohort if they had infections other than TB, inflammatory disorders, malignancies, autoimmune conditions, bone marrow failure, or anemia.

BLOOD COLLECTION AND LABORATORY ANALYSIS

Blood samples were collected via venipuncture using a disposable syringe. The venipuncture site was disinfected with a 70% alcohol swab, and 3 mL of venous blood was drawn. Samples were transferred into purple-top tubes containing 15% EDTA K3 to prevent coagulation. The tubes were gently mixed and transported to the laboratory.

HEMATOLOGY ANALYSIS

Complete blood count (CBC) was performed within 24-48 hours using a hematology analyzer. Evaluated parameters included red blood cell count (RBC), hemoglobin concentration (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cell count (WBC) with differential (neutrophils, lymphocytes, monocytes, eosinophils, basophils), and platelet count (PLT).

BIOCHEMICAL ANALYSIS

Lipid profiles (total cholesterol, triglycerides, low-density lipoprotein [LDL], high-density lipoprotein [HDL]), liver function tests (LFTs) including alanine transaminase (SGPT/ALT), aspartate transaminase (SGOT/AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and bilirubin (total, direct, indirect), as well as urea and creatinine, were assessed using a fully automated analyzer.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 22. Descriptive statistics (means, standard deviations, frequencies, and percentages) were calculated. Paired t-tests were used to compare means between the TB patient and control groups and to assess changes before and after treatment. A p-value of < 0.05 was considered statistically significant. Associations between hematological and biochemical indices were also explored.

RESULTS

GENERAL CHARACTERISTICS OF TUBERCULOSIS PATIENTS

The demographic and anthropometric features of the 100 TB patients are summarized in Table I. The data showed a higher proportion of males (58%) compared to females (42%). The majority of patients (62%) belonged to the 17-19 years age group, followed by the 14-16 years group (28%). The sample was ethnically diverse, with Pashtoons (48%) and Baloch (41%) being the most represented. Body mass index (BMI) analysis revealed that 52% of patients had a normal BMI (18.6-24.9), while 29% were underweight (BMI ≤ 18.5). Socioeconomic examination showed that 72% of the patients belonged to the middle class.

Table I. General characteristics of *Mycobacterium tuberculosis* patients (N=100)

	Numbers (N=100)	Percentage (%)
Age Group		
13	10	10
14-16	28	28
17-19	62	62
Gender		
Male	58	58
Female	42	42
Social Class		
Lower	21	21.0
Middle	72	72.0
Higher	7	7.0
Ethnicity		
Baloch	41	41.0

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Pashtoon	48	48.0
Others	11	11.0
BMI (Body Mass Index)		
≤ 18.5	29	29.0
18.6 - 24.9	52	52.0
≥25	19	19.0

* Data on residence and water source are available in the source document but are summarized here for conciseness

COMPLETE BLOOD COUNT (CBC) ANALYSIS

CBC findings for the 100 TB patients are detailed in Table II. Regarding white blood cells, 60% had normal WBC counts, while 36% had leukocytosis (>10.0×10^9/µl). Neutrophil levels were normal in 75% of patients, with 25% showing neutrophilia (>80%). A significant proportion (58%) of patients had lymphopenia (<20%). Eosinophil counts were normal in 67% of cases. All patients had normal basophil counts.

Anemia was prevalent, with 79% of patients having low hemoglobin levels. Red blood cell counts were normal in 48% and low in 33%. Hematocrit was below normal in 77% of patients. Microcytosis (low MCV) was observed in 61% of patients, and low MCH was found in 75%. Platelet counts were normal in 61%, with thrombocytosis in 23% and thrombocytopenia in 16%.

Table II. Distribution of complete blood count (CBC) in TB patients (N=100)

Parameter	Category	Frequency	Percent (%)
HB	Low	79	79.0
	Normal	21	21.0
RBC	High	19	19.0
	Normal	48	48.0
	Low	33	33.0
HCT	Normal	23	23.0
	Low	77	77.0
MCV	Normal	39	39.0
	Low	61	61.0
MCH	Normal	25	25.0
	Low	75	75.0
WBC	High	36	36.0
	Normal	60	60.0
	Low	4	4.0
PLT	High	23	23.0
	Normal	61	61.0
	Low	16	16.0
NEUTR	High	25	25.0
	Normal	75	75.0
LYMPTs	High	1	1.0
	Normal	41	41.0
	Low	58	58.0
EOSINPs	High	10	10.0
	Normal	67	67.0
	Low	23	23.0

LIVER FUNCTION TEST (LFT) ANALYSIS

The results of LFTs are presented in Table III. Serum total bilirubin was normal in 84% of patients. While 74% of patients had normal SGPT/ALT levels, 26% showed elevation. ALP was raised in 55% of cases. GGT was within the normal range in 71% of patients, and SGOT/AST was elevated in 37%.

Table III. Distribution of liver function tests (LFTs) in TB patients (N=100)

Parameter	Category	Frequency	Percent (%)
S_T_BILIR	High	16	16.0
	Normal	84	84.0
SGPT_ALT	High	26	26.0
	Normal	74	74.0
ALK_PHOSTs	High	55	55.0

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

	Normal	44	44.0
	Low	1	1.0
GAMMA_GT	High	29	29.0
	Normal	71	71.0
SGOT_AST	High	37	37.0
	Normal	63	63.0

LIPID PROFILE, UREA, AND CREATININE ANALYSIS

Lipid profile, urea, and creatinine results are summarized in Table IV. Triglyceride levels were normal in 84% of patients, with 16% having hypertriglyceridemia. Total serum cholesterol was in the desirable range for 91% of patients. A notable finding was low HDL cholesterol in 63% of patients. LDL and VLDL levels were normal in the majority (86% and 85%, respectively). Urea was normal in 76% of patients, and creatinine was normal in 43%.

Table IV. Distribution of lipid profile, urea, and creatinine in TB patients (N=100)

Parameter	Category	Frequency	Percent (%)
UREA	High	17	17.0
	Normal	76	76.0
	Low	7	7.0
CREAT	High	35	35.0
	Normal	43	43.0
	Low	22	22.0
TRI_GLY	High	16	16.0
	Normal	84	84.0
SERUM_CHOLST	Desirable	91	91.0
	Borderline High	5	5.0
	High	4	4.0
HDL	Normal	37	37.0
	Low	63	63.0
LDL	Normal	86	86.0
	Borderline High	10	10.0
	High	1	1.0
	Very High	3	3.0
V_LDL	Normal	85	85.0
	High	15	15.0

STATISTICAL ANALYSIS OF HEMATOLOGICAL PARAMETERS

Descriptive statistics for CBC parameters in active TB patients are shown in Table V. The analysis showed that the mean values for hematocrit (2.77 ± 0.42), MCH (2.75 ± 0.44), and MCV (2.61 ± 0.49) were higher on the ordinal scale used, while platelet count (1.93 ± 0.62), WBC count (1.68 ± 0.55), and neutrophil count (1.75 ± 0.44) were lower.

Table V. Descriptive statistics of hematological parameters in TB patients

Variable	Minimum	Maximum	Mean	Std. Deviation
HB	2.00	3.00	2.2100	0.40936
RBC	1.00	3.00	2.1400	0.71095
HCT	2.00	3.00	2.7700	0.42295
MCV	2.00	3.00	2.6100	0.49021
MCH	2.00	3.00	2.7500	0.43519
MCHC	1.00	3.00	2.4000	0.66667
WBC	1.0	3.0	1.680	0.5483
PLT	1	3	1.93	0.624
NEUTR	1	2	1.75	0.435
LYMPTs	1	3	2.57	0.517
MONOTs	1	3	1.70	0.503
EOSINPs	1	3	2.13	0.562
BASPs	2	2	2.00	0.000

The comparison between the diseased and control groups, shown in Table VI, reveals highly significant differences ($p < 0.05$) for WBC, eosinophils (EOS), hemoglobin, neutrophils (NEUTs), basophils (BASO), HCT, MCH, lymphocytes, MCV, and PLTs.

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Table VI. Paired t-test comparison of hematological parameters between TB patients and controls (N=100 pairs)

Variables	Mean Difference	t-value	df	Sig. (2-tailed)
HB1 - HB2	-3.34	-12.6	99	0.000
RBC1 - RBC2	-0.21	-1.61	99	0.111
HCT1 - HCT2	-5.40	-6.71	99	0.000
MCV1 - MCV2	-6.80	-4.97	99	0.000
MCH1 - MCH2	-6.25	-8.28	99	0.000
MCHC1 - MCHC2	-3.66	-8.99	99	0.000
WBC1 - WBC2	1.98	2.75	99	0.007
PLT1 - PLT2	73.56	4.35	99	0.000
NEUTR1 - NEUTR2	18.56	10.19	99	0.000
LYMP1 - LYMP2	-18.10	-10.99	99	0.000
MONO1 - MONO2	1.08	1.52	99	0.132
EOSO1 - EOSO2	-0.78	-2.18	99	0.031
BASO1 - BASO2	0.10	3.00	99	0.003

DISCUSSION

Tuberculosis remains one of the world's deadliest infectious diseases, causing significant morbidity and mortality (19, 20). The disease burden has seen a concerning increase, with a substantial proportion of cases concentrated in Asian countries, including Pakistan (21, 22). While industrialized nations have seen a decline in TB cases due to public health measures, low-income countries and marginalized populations continue to bear a disproportionate burden (23, 24). Teenagers represent a highly vulnerable group due to various biological and social factors, motivating the focus of this study.

In our study, TB was more prevalent in the 17-19 years age group (62%) and in males (58%). This finding aligns with other epidemiological studies. Pervin et al. (2024) found a higher prevalence of EPTB in individuals aged 11-18 years, though they reported a higher rate in females (25). Conversely, Aidarbek *et al.* (2022) reported a higher prevalence of pulmonary TB in females (65.3%) than in males (42.8%) (26). Gender disparity observed in our study may reflect differences in healthcare-seeking behavior, exposure, or biological susceptibility within the specific cultural context of Balochistan.

Nutritional status is a critical factor in TB pathogenesis (27). Our study found that a significant proportion of patients had a normal-to-low BMI, with 29% being underweight. This is consistent with the established link between TB and weight loss. While obesity rates are rising globally, underweight remains a significant problem in regions like South Asia, and this nutritional deficiency is a key risk factor for TB (28, 29). The inverse relationship between obesity and TB highlights the importance of nutritional status in disease development (30, 31). In a study by Dubois et al. (2022), a high percentage of children with TB were found to be underweight, reinforcing our findings (32).

Hematological abnormalities are a common feature of TB infection (33). These derangements, affecting both cellular and plasma components, can be exacerbated by anti-TB therapy (34, 35). In our study, we observed a spectrum of hematological findings. The presence of leukocytosis in 36% of patients reflects the systemic inflammatory response to infection. The significant lymphopenia observed in 58% of patients is a notable finding, as it may indicate immunosuppression or T-cell dysfunction, which is a hallmark of active TB. The high prevalence of anemia (79%) is a classic finding in chronic infectious diseases like TB, often attributed to anemia of chronic disease, nutritional deficiencies, or the infection itself.

The comparison between TB patients and controls (Table VI) revealed significant differences in most CBC parameters, underscoring the profound impact of the disease on hematopoiesis and the systemic inflammatory state. The lack of significant difference in RBC and monocyte counts in this paired analysis suggests that while these parameters are affected, their variability or the study's power might have limited the detection of a statistically significant difference. These findings emphasize the importance of thorough hematological monitoring for accurate diagnosis and follow-up of TB patients.

Recent years have seen a growing interest in the relationship between cholesterol and infectious diseases. While modern treatment protocols focus on lowering serum cholesterol to prevent cardiovascular disease, emerging evidence suggests a link between low serum cholesterol and conditions like TB (36).

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Alterations in lipid profiles are known to occur during TB infection, with an initial fall in total cholesterol (TC) and HDL followed by a rise in triglycerides (TGs) (37). Low HDL levels, a strong independent risk factor for poor cardiovascular outcomes, are also observed in TB patients (38-40).

Our study revealed a significant prevalence of dyslipidemia. Low HDL cholesterol was found in 63% of patients, and hypertriglyceridemia in 16%. These findings suggest a state of metabolic dysregulation that may contribute to the pathogenesis of the disease and have long-term cardiovascular implications for survivors. Furthermore, we noted abnormalities in renal markers, with 35% of patients having elevated creatinine, indicating potential renal involvement or dysfunction associated with the disease or its treatment.

A major concern associated with anti-tubercular therapy (ATT) is drug-induced hepatotoxicity (DIH) (36, 41). While many patients remain asymptomatic, subclinical hepatotoxicity is identified by changes in LFTs. In our study, elevated SGPT/ALT was observed in 26% of patients, and SGOT/AST was elevated in 37%. These elevations, particularly in ALT and AST, are key indicators of hepatocellular injury, commonly associated with first-line ATT drugs like isoniazid (INH) and rifampicin (RIF) (42, 43). Regular monitoring of LFTs is crucial for the early detection and prevention of hepatotoxicity. The lack of standardized protocols for managing DIH underscores the need for uniform guidelines to ensure patient safety without compromising the efficacy of treatment (44).

CONCLUSION

This study provides a comprehensive overview of the physiological and biochemical landscape in a cohort of teenage TB patients undergoing ATT in Balochistan. The results confirm that TB is associated with significant hematological derangements, including anemia, leukocytosis, and lymphopenia, which show significant differences compared to healthy controls. Furthermore, the study highlights a substantial burden of dyslipidemia, particularly low HDL, and a notable incidence of elevated liver enzymes, indicating subclinical hepatotoxicity.

Conflict of Interest:

Authors have no conflict of interest.

References:

1. Chakaya J, Khan M, Ntoumi F, Aklillu E, Fatima R, Mwaba P. Global Tuberculosis Report 2020 – Reflections on the Global TB burden, treatment and prevention efforts. Int J Infect Dis. 2021;113(Suppl 1):S7-S12.
2. Floyd K, Glaziou P, Houben R, Lönnroth K, Raviglione M. Global tuberculosis targets: are we on track? Eur Respir J. 2018;52(3):1801210.
3. Patterson B, Wood R. Is cough really necessary for TB transmission? Tuberculosis. 2019;117:31-5.
4. Yadav J, Prakash S. Transmission of tuberculosis: a review. Int J Res Med Sci. 2017;5(4):1178-82.
5. Kanabalan RD, Lee LJ, Lee TY, Chong PP, Hassan SA, Ismail R. Human tuberculosis and Mycobacterium tuberculosis complex: A review on genetic diversity, pathogenesis and omics approaches in host biomarkers discovery. Microbiol Res. 2021;246:126714.
6. Wiseman CA, Gie RP, Starke JR, Schaaf HS, Donald PR. A proposed radiological classification of childhood intra-thoracic tuberculosis. Pediatr Radiol. 2012;42(10):1165-73.
7. Pang Y, An J, Shu W, Huo F, Chu N, Gao M. Epidemiology of Extrapulmonary Tuberculosis among Inpatients, China, 2008–2017. Emerg Infect Dis. 2019;25(3):457-64.
8. Solovic I, Sester M, Gomez-Reino JJ, Rieder HL, Ehlers S, Milburn HJ. The risk of tuberculosis related to tumour necrosis factor antagonist therapies: a TBNET consensus statement. Eur Respir J. 2013;41(4):947-54.
9. Gopalaswamy R, Subbian S. Extrapulmonary Tuberculosis—An Update on the Diagnosis, Treatment and Drug Resistance. J Respir. 2021;1(2):141-64.
10. World Health Organization. Global tuberculosis report 2020. Geneva: World Health Organization; 2020.

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

11. Yong YK, Tan HY, Saeidi A, Wong WF, Vignesh R, Velu V. Immune Biomarkers for Diagnosis and Treatment Monitoring of Tuberculosis: Current Developments and Future Prospects. Front Microbiol. 2019;10:2789.
12. Moule MG, Cirillo JD. Mycobacterium tuberculosis Dissemination and Host Cell Death. In: Tuberculosis Host-Pathogen Interactions. Springer; 2020. p. 111-30.
13. Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis. 2016;63(7):e147-95.
14. Hillemann D, Rüsch-Gerdes S, Boehme C, Richter E. Rapid molecular detection of extrapulmonary tuberculosis by the automated GeneXpert MTB/RIF system. J Clin Microbiol. 2011;49(4):1202-5.
15. Malbruny B, Le Marrec G, Courageux K, Leclercq R, Cattoir V. Rapid and efficient detection of Mycobacterium tuberculosis in respiratory and non-respiratory samples. Int J Tuberc Lung Dis. 2011;15(4):541-5.
16. Golden MP, Vikram HR. Extrapulmonary tuberculosis: an overview. Am Fam Physician. 2005;72(9):1761-8.
17. Sharma SK, Ryan H, Khaparde S, Sachdeva KS, Singh AD, Mohan A. Index-TB Guidelines: Guidelines on extra-pulmonary tuberculosis for India. Indian J Med Res. 2021;153(4):417-42.
18. Marciano BE, Huang CY, Joshi G, Rezaei N, Carroll B, Zelazny AM. BCG vaccination in patients with severe combined immunodeficiency: complications, risks, and vaccination policies. J Allergy Clin Immunol. 2015;136(5):1381-3.
19. Arnadottir T. Tuberculosis: Trends in the disease and its control. In: Tuberculosis and Nontuberculous Mycobacterial Infections. 2009:3-12.
20. Ducati RG, Ruffino-Netto A, Basso LA, Santos DS. The resumption of consumption: a review on tuberculosis. Mem Inst Oswaldo Cruz. 2006;101(7):697-714.
21. Macdonald N, Harper I. Aetiology and epidemiology of tuberculosis. Medicine. 2019;47(10):609-13.
22. Shetty N, Shetty S. Epidemiology of tuberculosis. In: Tuberculosis. 2009:1-11.
23. Benjamin WH. Tuberculosis: a reemerging disease? In: Molecular Pathology of Lung Diseases. 2016:509-21.
24. Figueroa-Munoz JI, Ramon-Pardo P. Tuberculosis control in vulnerable groups. Bull World Health Organ. 2008;86(9):733-5.
25. Pervin S, Haque M, Shahidullah M, Mahmud T, Akhter S, Sultana N. Socio-demographic and clinical profile of children with tuberculosis in a tertiary care hospital in Bangladesh. J Tuberc Res. 2024;12(1):1-10.
26. Aidarbek A, Yerlan M, Rakhimova S, Chunkayeva Z. Epidemiological features of pulmonary tuberculosis among adolescents in Kazakhstan. Cent Asian J Glob Health. 2022;11(1):e534.
27. Tsabedze B. Nutritional status of patients with tuberculosis in a rural community in South Africa. S Afr J Clin Nutr. 2018;31(3):55-9.
28. Ford ND, Patel SA, Narayan KM. Obesity in low-and middle-income countries: burden, drivers, and emerging challenges. Annu Rev Public Health. 2017;38:145-64.
29. Yousaf M, Hameed T, Tahir M, Abbas F, Rafiq A, Khan A, Shah SH, Iqbal Q, Khan S, Rauf A, Rizwan M. Hemotological Study on Pulmonary Tuberculosis (PTB) Predominance in Quetta. Pak-Euro Journal of Medical and Life Sciences. 2019;2 (2):37-40.
30. Maro I, Mfinanga SG, Kirenga BJ, Byarugaba F, Mboera LE. Obesity and tuberculosis: a review. J Public Health Afr. 2010;1(1):e9.
31. Falagas ME, Kompoti M. Obesity and infection. Lancet Infect Dis. 2006;6(7):438-46.
32. Dubois MM, Brooks MB, Malik AA, Ahmed S, Hasan Z, Hussain H. Nutritional status of children with tuberculosis: a systematic review and meta-analysis. Nutr Rev. 2022;80(5):1074-88.
33. Abay F, Yalew A, Shibabaw T, Enawgaw B. Hematological abnormalities of pulmonary tuberculosis patients with and without HIV co-infection at the University of Gondar Hospital, Northwest Ethiopia: a comparative cross-sectional study. J Blood Med. 2018;9:51-8.
34. Kassa D, Enawgaw B, Gelaw A, Gelaw B. The effect of anti-tuberculosis treatment on hematological parameters in TB patients at Debre Tabor Hospital, Northwest Ethiopia: a retrospective cohort study. J Blood Med. 2016;7:161-8.
35. Tshikuka JG, Nzuzi JM, Bope M, Mvika B, Mumba D, Kayembe PK. Hematological changes in tuberculosis patients treated with rifampicin-containing regimen in Kinshasa, Democratic Republic of the Congo. Pan Afr Med J. 2014;19:374.

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

36. Tostmann A, Boeree MJ, Aarnoutse RE, de Lange WC, van der Ven AJ, Dekhuijzen R. Antituberculosis drug-induced hepatotoxicity: concise up-to-date review. J Gastroenterol Hepatol. 2008;23(2):192-202.
37. Deniz O, Tozkoparan E, Bozkanat E, Ciftci F, Bilgiç H, Ekiz K. Serum lipid profile in patients with tuberculosis. Tuberk Toraks. 2007;55(1):20-5.
38. Deniz O, Tozkoparan E, Ciftci F, Bozkanat E, Bilgiç H. The association between serum lipid profile and tuberculosis. Eur J Intern Med. 2006;17(5):331-5.
39. Pérez-Guzmán C, Vargas MH, Martínez-Rodríguez N, García-González A, Torres-Cruz A. Lipid profile in patients with tuberculosis: a systematic review and meta-analysis. Arch Med Res. 2005;36(5):512-8.
40. Iseki K, Yamazato M, Tozawa M, Takishita S. Hypocholesterolemia is a significant predictor of death in a cohort of chronic hemodialysis patients. Kidney Int. 2002;61(5):1883-9.
41. Lingaraju T, Rajeshwari KG, Shivaswamy KN. A study of drug-induced hepatotoxicity in patients on anti-tubercular therapy. Int J Basic Clin Pharmacol. 2015;4(6):1102-6.
42. Saukkonen JJ, Cohn DL, Jasmer RM, Schenker S, Jereb JA, Nolan CM. An official ATS statement: hepatotoxicity of antituberculosis therapy. Am J Respir Crit Care Med. 2006;174(8):935-52.
43. Chih HW, Lee CN, Lee YC. Isoniazid and rifampicin induced hepatotoxicity: a review. J Chin Med Assoc. 2014;77(5):227-31.
44. Wu SS, Chao CS, Vargas H, Sharp CW, Poon R, Liu H. A prospective study of drug-induced liver injury in patients receiving anti-tuberculosis treatment. J Formos Med Assoc. 2019;118(1 Pt 3):484-90.

Copyright © 2024 Authors. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.