Western European Journal of Medicine and Medical Science
Volume 3, Issue 09, September 2025
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

A MATHEMATICAL MODEL OF LATENT TUBERCULOSIS INFECTION PROGRESSION TO LOCALIZED TUBERCULOSIS IN CHILDREN FROM HOUSEHOLD TB FOCI IN UZBEKISTAN

Adjablaeva D.N., Parpieva N.N.
Samarkand State Medical University, Samarkand, Uzbekistan

Abstract
Background: Latent tuberculosis infection (LTBI) in children living in household TB contact settings remains a significant public health concern in high-incidence countries such as Uzbekistan. Although most infected children are asymptomatic, some progress to localized forms of tuberculosis, complicating both diagnosis and management.
Objective: To develop a prognostic mathematical model for assessing the risk of progression from LTBI to localized tuberculosis in children exposed to active TB cases within household contact environments in Uzbekistan.
Materials and Methods: A prospective cohort study was conducted with 120 children with confirmed LTBI from identified TB household contact settings. Clinical, immunological (including levels of IFN-γ, IL-2, IL-4), and social indicators were analyzed. A logistic regression model was used to build the predictive framework, and ROC analysis was applied to assess its diagnostic value.
Results: The most significant risk factors for disease progression included: acute respiratory infections, helminthic invasion, chickenpox, anemia, territorial TB focus, genitourinary diseases, ENT pathology, isoniazid monotherapy, COVID-19 exposure, IL-2 ≥ 251.1 ng/ml, and IgM ≥ 1.18 IU/ml. The model demonstrated high predictive accuracy (AUC = 0.769; 95% CI: 0.74–0.83).
Conclusions: The developed mathematical model enables early identification of children at high risk of progressing from LTBI to localized TB. Its application could improve screening strategies and preventive interventions in TB-endemic regions, particularly in Uzbekistan.
Keywords: Tuberculosis, Latent; Child; Tuberculin Test; Risk Factors; Interleukin-2; Cytokines; Immunity

Introduction

Latent tuberculosis infection (LTBI) in children remains a critical public health concern in countries with a high TB burden, such as Uzbekistan[1]. Although most children with LTBI remain asymptomatic, a notable proportion progress to localized or active forms of tuberculosis[2,3], particularly when specific biological, immunological, and social risk factors are present[4,5].

Children exposed to infectious TB cases within household settings are especially vulnerable due to their immature immune systems, close and prolonged contact with contagious individuals, and often adverse socioeconomic conditions[6,7]. This context poses significant diagnostic and prognostic challenges, as it remains unclear which children are at the greatest risk of disease progression[8,9].

Western European Journal of Medicine and Medical Science
Volume 3, Issue 09, September 2025
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

Despite advances in diagnostic technologies and immunological assessment, the current understanding of modifiable risk factors influencing LTBI progression in the pediatric population is still limited[10,11]. Identifying high-risk children and predicting disease progression remain essential for improving early intervention, guiding preventive treatment, and optimizing healthcare resource allocation[12].

The aim of this study is to develop a prognostic mathematical model that predicts the risk of progression from LTBI to localized tuberculosis in children living in household TB contact settings. The model incorporates clinical, epidemiological, immunological, and social determinants, and seeks to support targeted prevention strategies in endemic regions[13,14,15].

Materials and Methods

We conducted a prospective cohort study including 120 children diagnosed with latent tuberculosis infection (LTBI), all identified through confirmed household contact with active tuberculosis cases in Uzbekistan. The children were observed for 12 to 24 months and divided into two groups:

- Group 1 (n=40): LTBI progressed to localized TB
- Group 2 (n=80): LTBI remained stable without progression

Clinical data were collected along with social, epidemiological, and immunological parameters, including serum levels of cytokines (IFN-γ, IL-2, IL-4). Information about the source of infection (relation to child, bacillary status, drug resistance), BCG vaccination, comorbidities, family structure, housing conditions, and socioeconomic status was also recorded.

To evaluate the influence of multiple risk factors on disease progression, a binary logistic regression model was applied. This statistical method is suitable for analyzing the effect of various independent variables (mostly dichotomous) on a binary outcome — in our case:

1. LTBI progression to localized TB,
2. LTBI remaining without progression.

The model estimated adjusted odds ratios (ORs) and relative risks (RRs) with 95% confidence intervals. To assess the model's predictive ability, ROC (Receiver Operating Characteristic) curve analysis was performed, and the AUC (area under the curve) was calculated.

The study was approved by the Ethics Committee of the Samarkand State Medical University. Written informed consent was obtained from all parents or legal guardians.

Results

Out of the 120 children with latent tuberculosis infection (LTBI) observed over 12–24 months, 40 (33.3%) progressed to localized tuberculosis, while 80 (66.7%) remained clinically stable. Using binary logistic regression, we identified 12 independent predictors associated with progression (table1., table 2., table 3.).

Table 1. Predictors influencing the progression from LTBI to localized TB (based on data from the dispensary observation period)

No.	Predictor	B	Standard Error	Wald	p-value	Exp(B)
1	Acute respiratory infection (ARI)	-5.011	2.071	5.854	0.016	0.007
2	Helminthic invasion	-3.685	1.401	6.916	0.009	0.025
3	Chickenpox	-5.384	3.481	2.393	0.122	0.005

Western European Journal of Medicine and Medical Science
Volume 3, Issue 09, September 2025
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

No.	Predictor	B	Standard Error	Wald	p-value	Exp(B)
4	Anemia	-2.664	1.123	5.629	0.018	0.070
5	Territorial TB hotspot	0.920	1.625	0.320	0.571	2.509
6	Genitourinary diseases	-3.821	4.316	0.784	0.376	0.022
7	ENT pathology	-2.353	1.186	3.933	0.047	0.095
8	Isoniazid monotherapy	-5.844	2.455	5.667	0.017	0.003
9	Contact with COVID-19	-4.720	3.200	2.176	0.140	0.009
10	IL-2 ≥ 251.1 ng/ml	-1.258	1.997	5.872	0.027	0.077
11	IgM ≥ 1.18 IU/ml	-1.789	1.839	5.664	0.035	0.079
—	Constant	7.300	2.408	9.190	—	0.002

Table 2. Prognostic predictors for the outcome “progression to localized TB vs. no progression”

Predictor	Symbol	Logistic Regression Coefficient
Acute respiratory infection (ARI)	K_1	-5.011
Helminthic invasion	K_2	-3.685
Chickenpox	K_3	-5.384
Anemia	K_4	-2.664
Respiratory diseases (excluding ARI and TB)	K_5	0.920
Genitourinary diseases	K_6	-3.821
ENT pathology	K_7	-2.353
Acute intestinal infection (AII)	K_8	-5.844
Stress	K_9	-4.720
Surgical intervention	K_{10}	-4.292
IL-2 ≥ 1.035 ng/ml	K_{11}	-1.258
IgM ≥ 45.55 IU/ml	K_{12}	-1.789
Constant	K	7.300

Table 3. Coding Table for Predictive Variables in the Logistic Regression Model

No.	Coefficient (K)	Predictor	Code (X)
—	7.300	Constant (β)	—
1	-5.011	Acute respiratory infection (ARI)	X_1
2	-3.685	Helminthic invasion	X_2
3	-5.384	Chickenpox	X_3
4	-2.664	Anemia	X_4
5	0.920	Territorial TB hotspot	X_5

Western European Journal of Medicine and Medical Science
Volume 3, Issue 09, September 2025
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

No.	Coefficient (K)	Predictor	Code (X)
6	-3.821	Genitourinary diseases	X_6
7	-2.353	ENT pathology	X_7
8	-5.844	Isoniazid monotherapy	X_8
9	-4.720	COVID-19 exposure in household	X_9
10	-4.292	IL-2 ≥ 251.1 ng/ml	X_{10}
11	-1.258	IgM ≥ 1.18 IU/ml	X_{11}

These included clinical comorbidities (such as acute respiratory viral infections (ORVI), helminthic invasion, anemia, ENT pathology), immunological markers (elevated IL-2 ≥ 251.1 ng/ml and IgM ≥ 1.18 ME/ml), and social/environmental exposures (e.g., TB source case characteristics, territorial TB hotspots, COVID-19 exposure). Preventive treatment with isoniazid was associated with a significantly reduced risk of progression (Exp(B)=0.003; p=0.017).
The logistic regression model calculates the probability (P) of progression from latent tuberculosis infection (LTBI) to localized tuberculosis (TB) using the following formula:

$$p = 1/1+\exp^{(beta)}$$
$$\textbf{Beta} = -К + (К1 * X1) + (К2 * X2) + (К3 * X3) + (Кn * Xn)$$

K1, K2, etc. – coefficients of the logistic regression model
X1, X2, etc. – binary codes of the corresponding predictors (1, 2, etc.)

The final prognostic model achieved a classification accuracy of 96.3%, with sensitivity (Se) of 95.0% and specificity (Sp) of 97.5%. ROC curve analysis confirmed the model's discriminatory power with an AUC (Area Under the Curve) of 0.769, indicating acceptable model quality (Table4., figure 1.).

Table 4. Sensitivity and Specificity of the Applied Model

Observed Cases	Predicted Outcome	Correct Classification (%)
	LTBI → Localized TB	LTBI → No Progression
LTBI → Localized TB	38	2
LTBI → No Progression	1	39
Overall Classification Accuracy		

Note: Cut-off value = 0.500
Se = Sensitivity = TP / (TP + FN) = True Positives / (True Positives + False Negatives)
Sp = Specificity = TN / (TN + FP) = True Negatives / (True Negatives + False Positives)

Western European Journal of Medicine and Medical Science
Volume 3, Issue 09, September 2025
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

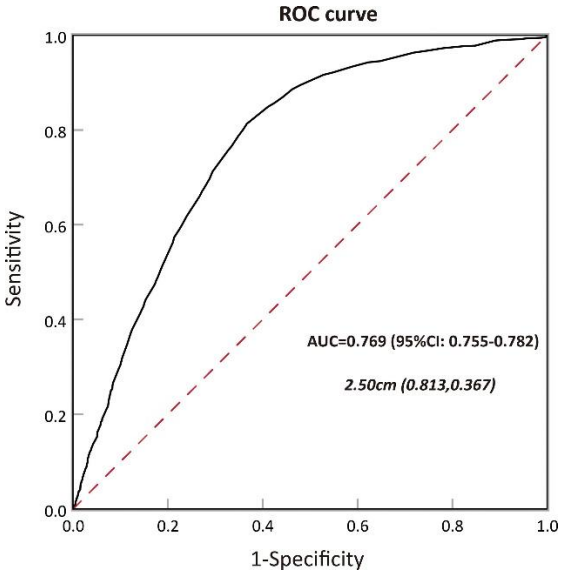

Figure 1. Receiver Operating Characteristic (ROC) curve for the prognostic model predicting progression from latent tuberculosis infection to localized tuberculosis in children

A practical scoring tool was constructed, assigning binary codes to each of the 12 predictors, allowing individualized risk calculation for LTBI progression in each child.

Discussion

This study reinforces the growing concern regarding pediatric progression from latent TB infection to active or localized disease, particularly in high-burden regions such as Uzbekistan[1,2]. Our findings highlight the multifactorial nature of LTBI progression, where biological, immunological, and social determinants interact to increase risk[3,4].

The logistic regression model developed here incorporated variables that are often overlooked in routine pediatric care, such as common viral infections (ORVI, varicella), parasitic diseases, and ENT pathologies — all of which showed significant associations with TB progression[5,6,7]. Elevated IL-2 and IgM levels were also found to be meaningful immunological predictors[8,9,10]. Mono-chemotherapy with isoniazid significantly reduced the likelihood of progression, underlining the importance of preventive therapy in children with confirmed LTBI[11]. The ROC analysis and overall model performance (Se 95.0%, Sp 97.5%, AUC 0.769) suggest that this model could be integrated into clinical workflows to support early identification of high-risk children[12,13].

The model's practical application in TB-endemic settings could help prioritize resources and interventions, particularly in under-resourced environments. However, its use requires validation in broader and more diverse populations[14,15].

Conclusions

The prognostic model developed in this study provides an evidence-based tool to predict the risk of LTBI progression in children exposed to TB within household settings[1,2]. With strong predictive performance and clinical relevance, it offers healthcare providers a reliable method for risk stratification, early intervention, and personalized preventive care in pediatric TB control programs[3,4].

Western European Journal of Medicine and Medical Science
Volume 3, Issue 09, September 2025
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

The inclusion of clinical, immunological, and social predictors such as cytokine profiles (IL-2, IgM), common childhood infections, and environmental conditions contributes to the model's utility in real-world settings[5,6]. Preventive treatment with isoniazid remains essential and was confirmed as a protective factor[7,8].
Further multicenter validation is recommended to generalize the application of this tool across diverse populations and strengthen early TB prevention strategies[9,10].

References

1. World Health Organization. *Global Tuberculosis Report 2023*. Geneva: WHO; 2023.
2. Getahun H, Matteelli A, Chaisson RE, Raviglione M. Latent *Mycobacterium tuberculosis* infection. *N Engl J Med*. 2015;372(22):2127–35.
3. Seddon JA, Shingadia D. Epidemiology and disease burden of tuberculosis in children: a global perspective. *Infect Drug Resist*. 2014;7:153–65.
4. Lewinsohn DA, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, et al. Official ATS/IDSA/CDC clinical practice guidelines: diagnosis of tuberculosis in adults and children. *Clin Infect Dis*. 2017;64(2):111–15.
5. Latorre I, Mialdea I, Serra-Vidal MM, Altet N, Prat C, Lacoma A, et al. Immune tools for the diagnosis of latent tuberculosis infection. *Expert Rev Anti Infect Ther*. 2015;13(12):1389–404.
6. Chee CBE, Reves R, Zhang Y, Belknap R. Latent tuberculosis infection: opportunities and challenges. *Respirology*. 2018;23(10):893–900.
7. Tsolia MN, Kanariou MG, Karpathios T, Syriopoulou VP. Cytokines in childhood tuberculosis. *Mediators Inflamm*. 1998;7(2):109–12.
8. Kampmann B, Tena-Coki G, Nicol M, Levin M. Investigating the immune response to *Mycobacterium tuberculosis* in children. *Am J Respir Crit Care Med*. 2006;174(9):987–93.
9. Dheda K, Barry CE, Maartens G. Tuberculosis. *Lancet*. 2016;387(10024):1211–26.
10. Martínez L, Cords O, Horsburgh CR, Andrews JR. The risk of tuberculosis in children after close exposure: a systematic review and individual-participant meta-analysis. *Lancet*. 2020;395(10228):973–84.
11. Mahomed H, Ehrlich R, Hawkridge T, Hatherill M, Geiter L, Kafaar F, et al. Diagnostic accuracy of T-cell-based assays for detecting *Mycobacterium tuberculosis* infection in children: a systematic review. *Pediatr Infect Dis J*. 2009;28(8):695–700.
12. Lee K, Kim HR, Lee SY, Choi HJ, Kang YA, Park SY, et al. Diagnostic performance of a cytokine biosignature in patients with latent tuberculosis infection. *Sci Rep*. 2020;10(1):20030.
13. Mandalakas AM, Kirchner HL, Walzl G, Galli L, Blakemore A, Hesseling AC. Optimizing the detection of recent tuberculosis infection in children. *Pediatrics*. 2015;135(6):e1649–59.