

ORIGINAL ARTICLE

Initiation of Isoniazid Preventive Therapy in Under-Five Children: A Cross-Sectional Study in Zambia

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ABSTRACT

Background: Tuberculosis (TB) is a preventable disease among children exposed to infection. Despite the World Health Organization's (WHO) recommendation for Isoniazid (INH) preventive therapy, TB remains prevalent, with 1.1 million global cases reported in 2022. In Zambia, the TB incidence stands at 307 cases per 100,000 people, with stigma and delayed diagnosis posing significant barriers to prevention efforts.

Objective: This study aimed to assess the prevalence of INH initiation and its associated factors among children under five attending four selected public health facilities in Zambia between 2019 and 2021.

Method: A cross-sectional study was conducted with 421 participants from four public health facilities. Data were collected using a structured checklist and analysed using STATA 16.1 MP

software. Binomial logistic regression was applied to obtain unadjusted and adjusted estimates at a 5% significance level.

Results: Higher education was identified as a protective factor for INH initiation (AOR=0.41, 95% CI: 0.20–0.83, p=0.013). Religious practice significantly increased the likelihood of initiation (AOR=19.2, 95% CI: 2.50–147.7, p=0.005), whereas stigma reduced the odds of initiation (AOR=0.46, 95% CI: 0.24–0.91, p=0.025), underscoring its negative impact.

Conclusion: INH initiation in children is significantly influenced by religious practices and community attitudes toward TB. To enhance uptake, targeted interventions should focus on addressing stigma, improving health education, and fostering community support for TB prevention efforts. However, the study is limited by its cross-sectional design, which does not establish causality, and the reliance on facility-based data, which may not capture broader community-level factors.

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INTRODUCTION

Tuberculosis (TB) remains a leading cause of morbidity and mortality among young children, particularly those living with adults who have pulmonary TB. The risk of TB infection in these children can be significantly reduced through preventive measures such as Isoniazid Preventive Therapy (IPT). The World Health Organization (WHO) recommends administering IPT for six months to asymptomatic child contacts under five years old to prevent TB development.¹ Studies have shown that IPT reduces TB risk by 59% in children under 14 years.² Despite this, IPT implementation remains suboptimal globally, including in Zambia.³ Globally, TB preventive therapy faces several challenges, including gaps in the identification, screening, initiation, and adherence among child contacts. In 2022, an estimated 1.1 million TB cases occurred in children, yet many eligible children did not receive IPT due to barriers such as stigma, limited healthcare worker capacity, poor drug supply chains, and diagnostic limitations.⁴ Zambia reported a TB incidence rate of 307 per 100,000 population in 2022, placing it among the high-burden countries. However, comprehensive data on IPT uptake and completion rates among children remain limited.⁵

Evidence from studies conducted in Lusaka and Solwezi districts shows that a considerable number of child contacts miss the opportunity to be screened or initiated on IPT, despite presenting at healthcare facilities.⁶ The WHO End TB Strategy underscores IPT as a core strategy for paediatric TB prevention, yet implementation in Zambia has encountered multiple systemic and community-level barriers.⁷ These include inadequate training of healthcare workers on IPT guidelines, erratic supply of isoniazid and pyridoxine, poor contact tracing and follow-up, and persistent stigma and misconceptions surrounding TB and its prevention.^{7,8,9,10} Paediatric TB diagnosis presents an additional challenge, primarily due to difficulties in sputum sample collection and reliance on smear microscopy, which has low sensitivity in children.¹¹

Although more sensitive tools such as Xpert MTB/RIF and Xpert MTB/RIF Ultra are available, their cost and limited availability restrict widespread use in resource-limited settings like Zambia.¹²

Internationally, IPT uptake and adherence vary widely. In Gambia, for instance, 78% of eligible children were initiated on IPT, with 61% completing the full six-month regimen.¹³ Conversely, in some high-burden settings, only 15% of eligible children initiate and complete at least four months of IPT.¹⁴ In Ethiopia, the integration of IPT into routine child health services was both feasible and acceptable, demonstrating improved uptake.¹⁵ Similarly, in South Africa, community-based approaches significantly enhanced IPT coverage and reduced TB incidence among exposed children.¹⁶ In Zambia, childhood TB often comes to clinical attention only after the diagnosis of TB in adult household contacts, resulting in missed opportunities for preventive interventions.¹⁷ National surveillance data indicate that children accounted for 10% of TB cases reported between 2004 and 2011.¹⁸ While notification rates declined from 135 per 100,000 in 2004 to 69 per 100,000 in 2010, the low reported burden among children likely reflects significant underdiagnosis and underreporting.^{19,20} These findings highlight an urgent need to assess IPT implementation, address barriers, and strengthen strategies aimed at improving access, adherence, and documentation. Strengthening these aspects within Zambia's public health framework is essential for reducing TB-related morbidity and mortality in children under five years.²¹

MATERIALS AND METHODS

Study Design and Setting

The study was an analytical cross-sectional study conducted in Solwezi district, Northwestern Province of Zambia. Solwezi is the capital of Northwestern Province and is located approximately 177 kilometres northwest of Chingola along the Chingola-Solwezi-Mwinilunga Road. This district was chosen due to its high tuberculosis (TB) burden, making it a relevant

setting for assessing isoniazid preventive therapy (IPT) initiation.

Four public health facilities were purposively selected from the thirteen available in the district. The selection was based on their high TB case load, geographical representation, and accessibility to ensure a diverse sample reflective of the broader district population.

Eligibility Criteria

The study included consenting parents/guardians who accessed TB care services and had at least one under-five child under their care between 2019 and 2021. Participants who were newly diagnosed with TB during the data collection period or were too sick to provide reliable information were excluded from the study to ensure data accuracy and consistency.

Study Variables

The outcome variable was the initiation of under-five children on IPT, categorized as a binary variable: Yes (1) for initiation or No (0) for non-initiation. Independent variables included demographic characteristics (gender, age, level of education, socioeconomic status), psychosocial factors (stigma, customs and beliefs, attitude towards TB prophylaxis, religion), and healthcare-related factors (availability and quality of health services).

Sampling and Sample Size

A simple random sampling method was used to select four health facilities out of the thirteen in the district. The study employed probability sampling to ensure representativeness and minimize selection bias. A total of 421 participants were sampled, with approximately 105 participants per facility.

The sample size was determined through power analysis to ensure sufficient statistical power for detecting associations between independent variables and IPT initiation. The calculation was based on expected prevalence rates of IPT initiation, a confidence level of 95%, and a margin of error of 5%. The OPD presumptive TB registers from TB

clinics served as the sampling frame, allowing for systematic participant selection.

Data Collection and Bias Minimization

Data were collected using structured interviewer-administered questionnaires. Interviewers were trained to standardize data collection procedures, reduce interviewer bias, and ensure reliability and validity. The questionnaires were pretested in a similar setting outside the study facilities, and necessary modifications were made based on the pretest findings. Additionally, data collection tools were designed to capture comprehensive demographic, psychosocial, and healthcare-related factors affecting IPT initiation.

To minimize selection bias, participants were randomly selected from the presumptive TB registers, and efforts were made to include respondents from diverse backgrounds within the district. Recall bias was minimized by restricting data collection to a specific timeframe (2019–2021) and using facility records to verify participant responses.

Ethical considerations

Ethics clearance was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) (REF. No. 1461-2021). Permission to proceed with the study was also granted by the National Health Research Authority (NHRA) (Ref No: NHRA0000011/26/05/2021), the Provincial Health Office (PHO), and the District Health Office (DHO). Further approval was obtained from each health facility in-charges. Written informed consent was obtained from all participating parents and guardians before data collection, ensuring that they fully understood the study's purpose, risks, and benefits. Confidentiality was maintained by anonymizing participant data and securely storing all research records. Throughout the study, the researcher adhered to the principles of ethical research conduct, including justice, beneficence, and respect for human dignity.

Statistical analysis

Data were analysed using STATA version 16.1 MP (StataCorp, College Station, TX, USA). Contingency tables were used to compare the distribution of categorical variables between children who were initiated on INH and those who were not. The Pearson chi-square test used to test for associations between study variables. The odds of INH initiation, p-values, and associated 95% confidence intervals (CIs) were estimated using unadjusted and adjusted binomial logistic regression analysis. An investigator-led backward stepwise approach was adopted in model development. The likelihood ratio test, AIC, and BIC statistics were used to pick between competing models. A complete case analysis approach was adopted in the analysis process and all statistical analyses were done at a 5% level of significance.

RESULTS

Comparison of Baseline Characteristics between levels of INH initiation

The study was conducted on a sample of 421 participants. Table 1 shows that most participants, 304 (72.2%) were female, with under two-thirds aged between 35 and 54 years 254 (60.3%). About three-quarters, 325 (77.2%) were from low-cost areas. Slightly over half, 218 (51.8%) attained at least a secondary level education. Most of the participants, 306 (80.7%) practiced some form of religion and over half, 184 (57.7%) reported experiencing stigma from the community. Over a quarter, 93 (27.8%) had no trust in the health care provided to their child. A large proportion, 320 (84.7%) of the participants reported having customs/beliefs that influenced seeking TB treatment for their child. Most participants, 291 (73.7%) were from communities with negative beliefs towards TB.

Table 1: Parents and guardians' socio-demographic characteristics (n=421)

Characteristic	Category	Overall n (%)	Initiated on Isoniazid	
			Yes, n (%)	No, n (%)
Gender	Female	304 (72.2)	52 (17.1)	252 (82.9)
	Male	117 (27.8)	30 (25.6)	87 (74.4)
Age group	17 – 34 years	141 (33.5)	24 (17.0)	117 (83.0)
	35 – 54 years	254 (60.3)	54 (21.3)	200 (78.7)
	Over 54 years	26 (6.2)	4 (15.4)	22 (84.6)
Residence	Low cost	325 (77.2)	67 (20.6)	258 (79.4)
	Medium cost	96 (22.8)	15 (15.6)	81 (84.4)

Characteristic	Category	Overall n (%)	Initiated on Isoniazid	
			Yes, n (%)	No, n (%)
Education level	= Primary	203 (44.2)	47 (23.2)	156 (76.9)
	= Secondary	218 (51.8)	35 (16.1)	183 (83.9)
Religious practice	Yes	306 (80.7)	71 (23.2)	235 (76.8)
	No	73 (19.3)	6 (8.2)	67 (91.8)
Experience of stigma	Yes	184 (57.7)	32 (17.4)	152 (82.6)
	No	135 (42.3)	32 (23.7)	103 (76.3)
Trust in care provided	Yes	242 (72.2)	53 (21.9)	189 (78.1)
	No	93 (27.8)	21 (22.6)	72 (77.4)
Influence of customs/beliefs	Yes	320 (84.7)	61 (19.1)	259 (80.9)
	No	58 (15.3)	7 (12.1)	51 (87.9)
Community's attitude towards TB	Negative	291 (73.7)	0 (0.0)	291 (100.0)
	Positive	104 (26.3)	82 (78.9)	22 (21.2)

The study was conducted on a sample of 421 participants. Table 2 shows that most participants, 304 (72.2%) were female, with under two thirds aged between 35 and 54 years 254 (60.3%). About three quarters, 325 (77.2%) were from low-cost areas. Slightly over half, 218 (51.8%) attained at least a secondary level education. Most of the participants, 306 (80.7%) practiced some form of religion and over half, 184 (57.7%) reported experiencing stigma from the community. Over a quarter, 93 (27.8%) had no trust in the health care

provided to their child. A large proportion, 320 (84.7%) of the participants reported having customs/beliefs that influenced seeking TB treatment for their child. Most participants, 291 (73.7%) were from communities with negative beliefs towards TB. Initiation of under-five children on isoniazid in the three-year period was significantly associated with religious practice ($p=0.004$) and community attitudes towards Tuberculosis infection ($p<0.0001$).

Table 2: Parents and guardians' Bivariant characteristics (n=421)

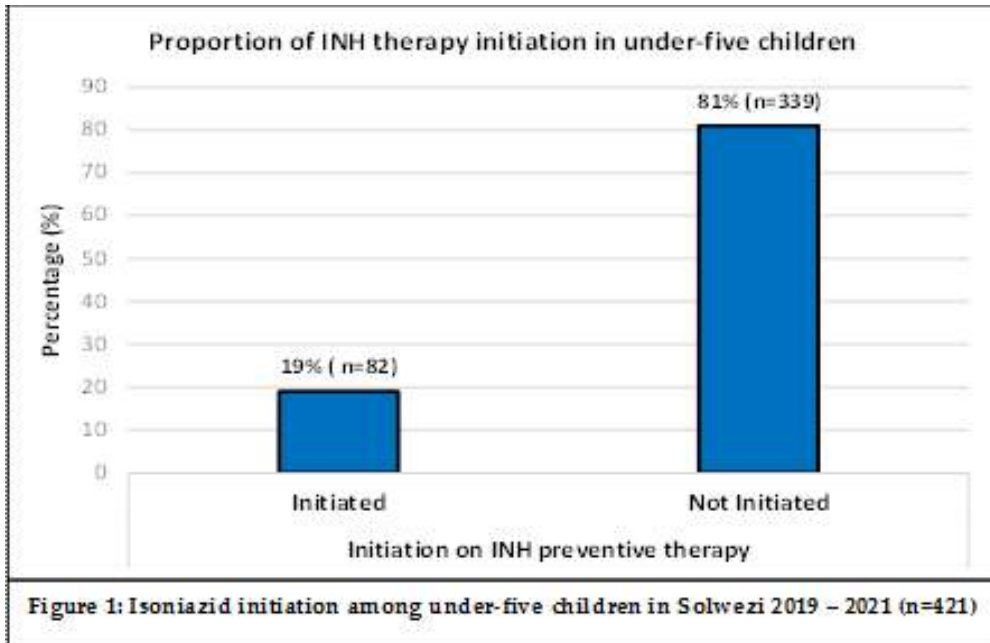
Characteristic	Category	Overall n (%)	Initiated on Isoniazid		P-value
			Yes, n (%)	No, n (%)	
Gender	Female	304 (72.2)	52 (17.1)	252 (82.9)	0.048 ^{CH}
	Male	117 (27.8)	30 (25.6)	87 (74.4)	
Age group	17 – 34 years	141 (33.5)	24 (17.0)	117 (83.0)	0.513 ^{CH}
	35 – 54 years	254 (60.3)	54 (21.3)	200 (78.7)	
	Over 54 years	26 (6.2)	4 (15.4)	22 (84.6)	
Residence	Low cost	325 (77.2)	67 (20.6)	258 (79.4)	0.278 ^{CH}
	Medium cost	96 (22.8)	15 (15.6)	81 (84.4)	
Education level	Primary	203 (44.2)	47 (23.2)	156 (76.9)	0.003 ^{CH}
	Secondary	218 (51.8)	35 (16.1)	183 (83.9)	
Religious practice	Yes	306 (80.7)	71 (23.2)	235 (76.8)	0.004 ^{CH}
	No	73 (19.3)	6 (8.2)	67 (91.8)	
Experience of stigma	Yes	184 (57.7)	32 (17.4)	152 (82.6)	0.164 ^{CH}
	No	135 (42.3)	32 (23.7)	103 (76.3)	
Trust in care provided	Yes	242 (72.2)	53 (21.9)	189 (78.1)	0.893 ^{CH}
	No	93 (27.8)	21 (22.6)	72 (77.4)	
Influence of customs/beliefs	Yes	320 (84.7)	61 (19.1)	259 (80.9)	0.202 ^{CH}
	No	58 (15.3)	7 (12.1)	51 (87.9)	
Community's attitude towards TB	Negative	291 (73.7)	0 (0.0)	291 (100.0)	< 0.0001 ^{CH}
	Positive	104 (26.3)	82 (78.9)	22 (21.2)	

CH = Chi square test

Initiation of under-five children on INH preventive therapy

As shown in Figure 1, the initiation of under-five children on INH preventive therapy between 2019

and 2021 in Solwezi district was low 82 (19%), with the majority, 339 (81%) of participants having not had their under-five children initiated on Isoniazid.



Factors influencing the initiation of under-five children on INH preventive therapy

Table 3 in adjusted analysis shows that male respondents had higher odds of the outcome compared to females, but this association was not statistically significant (AOR = 1.48, CI = 0.74, 2.96, P = 0.264). Participants with secondary education or higher had significantly lower odds of the outcome compared to those with primary education or less, indicating a 59% reduction in odds (AOR = 0.41, CI = 0.20, 0.83, P = 0.013). Those who practiced religion had 19

times higher odds of the outcome compared to those who did not, and this effect was statistically significant (AOR = 19.2, CI = 2.50, 147.7, P = 0.005). Additionally, respondents who experienced stigma had significantly lower odds of the outcome, with a 54% reduction observed (AOR = 0.46, CI = 0.24, 0.91, P = 0.025). Other variables such as age group, residence, trust in care provided, and customs and beliefs were not statistically significant in the unadjusted analysis.

Table 3: Unadjusted and adjusted logistic regression analysis estimates (n=421)

Variables	Unadjusted estimates			Adjusted estimates		
	cOR	CI (95%)	P-Value	AOR	CI (95%)	P-Value
Gender						
Female	Ref			Ref		
Male	1.67	1.00, 2.79	0.049	1.48	0.74, 2.96	0.264
Age group						
17 – 34 years	Ref			Ref		
35 – 54 years	1.32	0.77, 2.24	0.312			
> 54 years	0.89	0.28, 2.81	0.837			
Residence						
Low	Ref			Ref		
Medium	0.71	0.39, 1.32	0.280			
Education level						
Primary	Ref			Ref		
Secondary	0.63	0.39, 0.93	0.017	0.41	0.20, 0.83	0.013
Religious practice						
No	Ref			Ref		
Yes	3.37	1.40, 8.10	0.007	19.2	2.50, 147.7	0.005
Experience of stigma						
No	Ref			Ref		
Yes	0.68	0.39, 0.97	0.006	0.46	0.24, 0.91	0.025
Trust in care provided						
No	Ref			Ref		
Yes	0.96	0.54, 1.71	0.893			
Customs and beliefs						
No	Ref			Ref		
Yes	1.72	0.74, 4.00	0.207			

cOR= Crude Odds Ratio, cOR= Adjusted Odds Ratio, CI= Confidence Interval

DISCUSSION

The study investigated the initiation of isoniazid (INH) preventive therapy among under-five children and the various factors influencing its uptake. The results revealed a concerning trend in healthcare-seeking behaviour, with more females than males actively involved in pursuing care for their under-five children. This gender dynamic is essential in understanding the broader sociocultural landscape of healthcare, especially in many low- and middle-income countries (LMICs), where women often play a primary role in child health decisions.^{1,22} Women's active participation is critical, as studies have shown that maternal education levels and their health beliefs directly affect the health-seeking behaviour for children.^{23,24} This finding aligns with studies from Ethiopia and Nigeria, where maternal influence was a key determinant of child health interventions.^{23,25,26}

Despite the role of caregivers, the study found the initiation rate of INH therapy for children under five was alarmingly low, with only 19 percent of participants reporting that their children had begun treatment between 2019 and 2021. This initiation rate is significantly lower than recommended targets set by global health bodies. The World Health Organization (WHO) recommends that all eligible children under five living in households of patients with TB should receive IPT immediately.^{1,27} A similar study in South Africa found that IPT uptake was higher in urban settings compared to rural areas due to better healthcare access.²⁷ Clearly, the gap between recommended practices and actual outcomes needs urgent attention, and policies should focus on improving access to IPT, particularly in rural and underserved areas.

The findings also highlighted the impact of religious beliefs on IPT initiation. Some communities view TB as a spiritual affliction rather than a medical condition, leading individuals to seek faith-based healing rather than biomedical treatment. This belief can discourage the uptake of IPT. Additionally, TB is often associated with HIV in many communities, and due to the stigma

surrounding HIV/AIDS, individuals may fear being labelled as HIV-positive if diagnosed with TB. This fear may lead families to conceal exposure history and avoid preventive treatment. Religious beliefs influencing healthcare decisions have also been reported in studies from Nigeria, where faith-based healing practices were found to delay TB treatment initiation.^{10,27} Further research is needed to develop culturally sensitive health education programs that address these concerns while respecting religious beliefs.

Community attitudes towards tuberculosis (TB) were another major factor affecting IPT initiation. Attitudes towards TB, which may be influenced by stigma and misunderstanding about the disease, have been shown to significantly affect treatment-seeking behaviour.²⁸ For instance, a study conducted in South Africa in 2018 found that caregivers who harboured negative beliefs about the side effects of INH therapy were notably less likely to initiate such preventive measures for their children.²⁸ The stigma associated with TB can result in families withholding information regarding potential exposure to TB or even the importance of preventive measures. This perpetuates cycles of transmission and negative health outcomes within communities. Policy interventions should focus on integrating stigma reduction strategies into TB awareness campaigns and healthcare provider training.²⁸

Inadequate and incomplete record-keeping was also identified as a major barrier to the low initiation rates observed in this study. Prior research has revealed that poor documentation and tracking of patients receiving preventive therapy contribute to difficulties not only in treatment initiation but also in monitoring and evaluating health programs.^{9,28} This observation aligns with the findings from Kenya in 2017, where researchers indicated that the lack of clear guidelines for IPT implementation was significantly detrimental.^{9,29} A study in Ethiopia similarly found that weak health information systems led to gaps in IPT monitoring, reinforcing the need for improved data collection processes.²⁹

Given that record-keeping is foundational to healthcare delivery, the deficiencies highlighted in this study underscore an urgent need for improved healthcare information systems to enhance the monitoring of medication initiation.

The literature further indicates drug availability as another critical factor impacting the initiation of IPT among eligible children. A comprehensive community-based study from India showed that even when guidelines were clear, the irregular supply of INH often hampered delivery, suggesting that supply chain weaknesses should be a primary focus alongside educational efforts.^{8,29} Similar reports have emerged from South Africa, highlighting that only 265 out of 525 eligible children received IPT, due partially to an inconsistent drug supply.^{27,29} In Nigeria, drug stockouts were reported as a leading cause of IPT discontinuation.³⁰ Such supply chain issues exacerbate existing disparities in healthcare access, particularly for at-risk populations like children under five years old. Strengthening supply chain management and ensuring consistent availability of IPT drugs should be prioritized in policy reforms.³⁰

Moreover, healthcare workers' limited knowledge regarding IPT represents a crucial barrier to effective implementation. A study in Zambia highlighted that many healthcare workers lacked adequate training and knowledge about the importance of IPT, directly correlating with lower initiation rates.³¹ Conversely, a study in Ethiopia observed that healthcare workers who received training on IPT were more likely to initiate treatment in eligible children, suggesting that targeted training programs can substantially enhance program outcomes.^{23,30} This reaction aligns with broader findings showing that professional development and ongoing training are critical to delivering effective healthcare services.^{25,31} Policymakers should integrate IPT training into routine health worker capacity-building programs to improve service delivery and adherence to WHO guidelines.

Barriers identified in existing studies also manifest as transportation costs, lack of knowledge among caregivers, and unavailability of diagnostic resources. For instance, research conducted in Malawi reported that such economic factors significantly hindered families' capacity to seek timely intervention.³² Similarly, a study in Ethiopia found that financial constraints, including indirect costs such as missed workdays, influenced caregivers' ability to seek timely IPT services.^{30,32} Lack of access to necessary diagnostic tests, including chest radiography or the Mantoux test, further complicates efforts to diagnose TB and initiate IPT.^{24,32} In Nigeria, evidence suggests that despite policy frameworks supporting TB prevention, poor healthcare infrastructure, particularly in rural areas, significantly impairs early diagnosis and treatment initiation.^{10,30} In areas of poverty, the additional burden of travel and financial obligations can deter families from utilizing available health services, culminating in an increase in missed opportunities for preventive therapies.^{1,30}

Exploring the multi-faceted barriers to the initiation of isoniazid among under-five children necessitates an understanding of not just healthcare systems but also community dynamics and caregiver perspectives. The study found that misconceptions surrounding TB and its treatment were prevalent, which led to hesitancy in accessing IPT services.^{10,32} This aligns with findings from South Africa, where researchers identified that a lack of awareness about the benefits of IPT among caregivers was a major contributor to low uptake.^{22,31} Education campaigns focusing on demystifying TB, addressing cultural beliefs, and reinforcing the safety and efficacy of preventive therapy could facilitate increased engagement from caregivers. Additionally, incorporating community health workers has shown promise in bridging gaps between families and healthcare services, providing localized support and increasing overall knowledge about TB prevention.^{23,29,32} Evidence from Ethiopia and

Nigeria suggests that community health workers who received TB-focused training were instrumental in increasing IPT uptake rates through active follow-ups and direct engagement with caregivers.^{24,26,30}

To emphasize the importance of implementing community-level interventions, one can refer to the missed opportunities in healthcare delivery that have been frequently documented in the literature. Studies from various LMICs suggest that systemic hurdles in healthcare delivery can significantly affect health outcomes for children, particularly those under five, who are considered a vulnerable population.^{22,32} Comparisons with WHO guidelines further highlight gaps in program implementation, as the global health body strongly recommends integrating IPT within routine child health programs to maximize accessibility and coverage.^{1,31,32} The intersection of community education efforts, improved healthcare worker training, and robust supply chain management emerges as a potent framework for enhancing the initiation of IPT among this demographic.³²

CONCLUSION

To strengthen the initiation and uptake of isoniazid preventive therapy (IPT) among under-five children, national TB programs should implement targeted community education initiatives to address misconceptions, stigma, and misinformation, while engaging community health workers to enhance caregiver knowledge. Healthcare provider training should be improved by integrating TB preventive therapy education into routine practice and strengthening mentorship programs. Ensuring a consistent supply of IPT drugs and diagnostic tools, alongside efficient monitoring frameworks, is crucial for effective implementation. Additionally, integrating IPT services into routine child healthcare visits, reducing financial and logistical barriers, and exploring home-based or community-based IPT distribution can enhance accessibility. Future research should incorporate mixed-methods studies to explore caregiver and healthcare provider perspectives, evaluate the effectiveness of

community-based interventions, and strengthen policy frameworks for integrating IPT into broader child health initiatives. By adopting these strategies, national TB programs can improve IPT accessibility, reduce childhood tuberculosis burden, and enhance overall child health outcomes.

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Informed Consent Statement: Informed consent was obtained from all study participants involved in the study.

Data Availability Statement: The data used and presented in this study are available on reasonable request from the corresponding author. The data are not publicly available due to the National Health Research Authority's legal and ethical restrictions.

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