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Towards the WHO target of zero childhood tuberculosis deaths: an analysis of mortality in 13 locations in Africa and Asia

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SUMMARY

SETTING: Achieving the World Health Organization (WHO) target of zero paediatric tuberculosis (TB) deaths will require an understanding of the underlying risk factors for mortality.

OBJECTIVE: To identify risk factors for mortality and assess the impact of human immunodeficiency virus (HIV) testing during anti-tuberculosis treatment in children in 13 TB-HIV programmes run by Médecins Sans Frontières.

DESIGN: In a retrospective cohort study, we recorded mortality and analysed risk factors using descriptive statistics and logistic regression. Diagnosis was based on WHO algorithm and smear microscopy.

RESULTS: A total of 2451 children (mean age 5.2 years, SD 3.9) were treated for TB. Half (51.0%) lived in Asia, the remainder in sub-Saharan Africa; 56.0% had pulmonary TB; 6.4% were diagnosed using smear microscopy; 211 (8.6%) died. Of 1513 children tested for HIV, 935 (61.8%) were positive; 120 (12.8%) died compared with 30/578 (5.2%) HIV-negative children. Risk factors included being HIV-positive (OR 2.6, 95%CI 1.6–4.2), age <5 years (1.7, 95%CI 1.2–2.5) and having tuberculous meningitis (2.6, 95%CI 1.0–6.8). Risk was higher in African children of unknown HIV status than in those who were confirmed HIV-negative (1.9, 95%CI 1.1–3.3).

CONCLUSIONS: Strategies to eliminate childhood TB deaths should include addressing the high-risk groups identified in this study, enhanced TB prevention, universal HIV testing and the development of a rapid diagnostic test.

KEY WORDS: HIV; co-infection; sub-Saharan Africa; paediatric

THERE HAS BEEN some success in controlling TB, with global rates of tuberculosis (TB) declining since 2004, but childhood TB remains a neglected area.[1] The World Health Organization (WHO) estimates that 6.7% of the 8.7 million people reported with TB in 2011 were children, of whom 64 000 died;[2] however, others have estimated that the global burden of paediatric TB is higher.[3]

There have been a number of calls to focus on paediatric TB.[4] Clinical trials of TB diagnosis and treatment in children are scarce, and published data are often from small cohorts with differing definitions of disease. International reporting to the WHO focuses on whole-cohort TB outcomes, recently moving to age-disaggregated data for case finding but not for outcome reports.[5] Sandgren et al. have shown that the incidence and outcomes of TB notified for patients aged <15 years in a cohort may not correlate well with the incidence and outcomes recorded for the overall cohort.[6] In addition, the limited published data on paediatric outcomes tend to originate from single-context studies where diagnosis and treatment protocols can vary. Mortality rates vary from 6% in Thailand[7] to 17% in Malawi.[8] However, similar risk factors for death are reported across these settings: younger age, smear negativity and human immunodeficiency virus (HIV) infection. In 2011 the WHO brought together international stakeholders who signed a call to action to tackle childhood TB. The aim is to reach zero childhood deaths from TB, which is a formidable task.[9] One crucial element to achieve this will be robust treatment of paediatric TB; it is therefore vital to identify the factors associated with mortality across multiple programmes and contexts.

For more than 5 years, Médecins Sans Frontières (MSF) has run integrated TB-HIV services, including treatment for children, in six countries (Central African Republic, Democratic Republic of Congo, Uganda, Zimbabwe, India and Myanmar) where HIV prevalence among children treated for TB was

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>5%. Treatment is provided per standardised protocols and data are routinely collected prospectively from all programmes.

The primary objective of the present study was to identify factors increasing the risk of death during anti-tuberculosis treatment in children aged <15 years. The secondary objective was to determine the impact of HIV testing, as part of TB care, on TB treatment outcomes in children.

STUDY POPULATION AND METHODS

Study design

We performed a retrospective multi-setting cohort study in 13 MSF programmes providing integrated TB-HIV care. We included all individuals aged <15 years in whom anti-tuberculosis medication had been initiated for a proven or presumptive diagnosis of TB during January 2007 to June 2010.

Definitions

The diagnosis of TB was based on standardised guidelines.[10] If a clinician suspected TB, the diagnosis was established using a combination of history, clinical assessment, paediatric scoring system (modified Crofton),[10] microscopy for acid-fast bacilli where sputum (or other bodily fluids) was obtainable and chest radiograph, if available. Patients were treated with a standardised drug regimen per WHO guidelines:[11] most patients received 2HRZE/4HR,* with the option for some patients in some projects of receiving 2HRZ/4HR, 4HRZE/6HE or 2SHRZE/1HRZE/5HRE. None of the programmes had implemented the 2010 rapid advice WHO guidelines recommending increased dosages of TB medications for children.[11] HIV testing was recommended as part of standard care. HIV care included cotrimoxazole prophylaxis, nutritional support, if appropriate, and antiretroviral therapy (ART).

The main outcome was death from any cause during anti-tuberculosis treatment. Additional data collected included demographic data, HIV status (tested using rapid antibody kits and confirmed by enzyme-linked immunosorbent assay if >18 months of age; in younger children the rapid antigen test was confirmed by viral load testing, where available, but some programmes relied on clinical diagnosis), clinical TB data (smear status, site of disease and any radiograph information) and treatment outcome (per WHO criteria).[11]

Clinical data collection

Each TB programme had been running for at least 1 year before data collection. Data were recorded prospectively in a standard format across all programmes and transferred to an electronic database (Microsoft Excel; Microsoft, Redmond, WA, USA) by project staff. Quality checks were performed through programme supervision and epidemiologist support. Anonymised individual level data were reported quarterly, in line with standard TB reporting.

Statistical analysis

Data analysis was performed using Stata 11 statistical software (StataCorp, College Station, TX, USA). Baseline characteristics of patients were described as proportions. The outcome variable was death from all causes during anti-tuberculosis treatment. Multiple exposures were considered to identify risk factors for death (age, sex, site of TB disease, HIV status and TB history). Univariate analysis was performed using logistic regression with odds ratios (ORs) and 95% confidence intervals (CIs). A random effects logistic regression model was created to account for the intracluster effect of the multisite study. We used a stepwise forward technique: variables were included in the order of strength of the crude association, and the likelihood ratio test was calculated for each step. Adjusted ORs (aORs) and 95%CIs were estimated. Where effect modification was identified, the effects were reported separately.

To achieve the secondary study objective, i.e., to study the impact of HIV testing on TB treatment outcome in children, children whose HIV status was not recorded were compared with HIV-negative children, the null hypothesis being that the groups were at the same risk of death during anti-tuberculosis treatment.

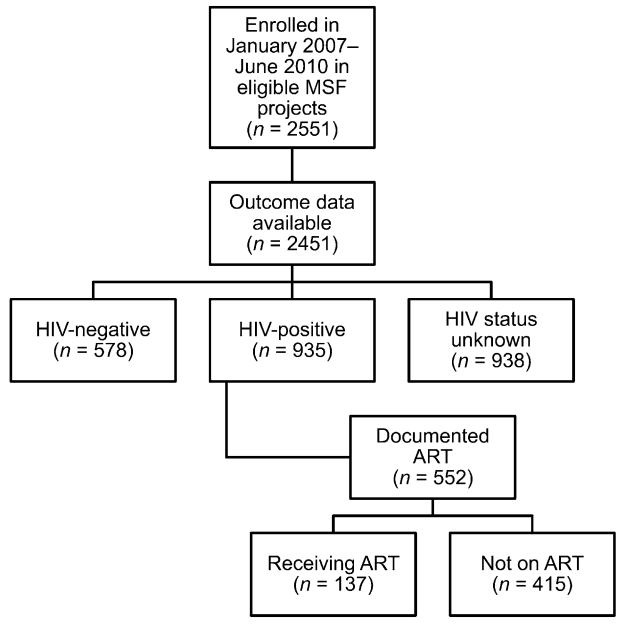

Figure Study population profile. MSF = Médecins Sans Frontières; HIV = human immunodeficiency virus; ART = antiretroviral therapy.

*H = isoniazid; R = rifampicin; Z = pyrazinamide; E = ethambutol; S = streptomycin. Numbers before the letters indicate the duration in months of the phase of treatment.

Ethics

This work met the criteria established by the MSF Ethics Review Board, Amsterdam, The Netherlands, for retrospective analysis of routine programme data, and received approval from the Ethics Committee of the London School of Hygiene & Tropical Medicine, London, UK.

RESULTS

From January 2007 to June 2010, 2551 children were enrolled in eligible MSF projects. Outcome data were available for 2451 children (Figure). There were almost equal numbers of children in treatment programmes in Asia (1250/2451, 51.0%) and sub-Saharan Africa (1201/2451, 49.0%; Table 1): 1425 children were aged 5–14 years and 1026 were <5 years (Table 1).

The majority (94.1%) of the children were new TB cases; 6.5% (n = 158) were smear-positive and 2.0% (n = 50) had tuberculous meningitis. Of the 937 children with extra-pulmonary TB, 283 (30.2%) had tuberculous lymphadenitis (Table 1).

HIV status was recorded as unknown in 938 (38.3%) children. Of children tested for HIV infection, 935 had a positive result and 578 tested negative (Figure). The proportion of children whose HIV status was unknown fell from 50.9% in 2007 to 25.0% in 2010 (data not shown); 77.7% of children were successfully treated (cured or completed), 241 (9.4%) defaulted before treatment completion (no statistically significant difference between HIV status groups) and 211 (8.6%) died during treatment (Table 2).

Compared with 30 (5.2%) HIV-negative children and 61 (6.5%) children with unknown HIV status, 120 (12.8%) HIV-positive children died (Tables 2 and 3). In univariate analysis, mortality from all causes was independently associated with age (OR 0.64, 95%CI 0.5–0.8), site of TB disease (OR 4.1, 95%CI 1.5–11.3), the child's place of residence (OR 0.6, 95%CI 0.5–0.8) and HIV status (OR 2.7, 95%CI 1.8–4.1, Table 3). There was no association with treatment regimen.

In multivariate analysis (of children with documented HIV status), HIV-positive children had increased odds of death compared with HIV-negative children (OR 2.6, 95%CI 1.6–4.2). Children aged

Table 1 Baseline characteristics (N = 2451)

Variable	n (%)
Sex	
Female	1195 (48.8)
Male	1256 (51.2)
Age group, years	
0–4	1026 (41.9)
5–14	1425 (58.1)
Year of enrolment	
2007	819 (33.4)
2008	825 (33.7)
2009	615 (25.1)
2010	192 (7.8)
Country	
Central African Republic (1 project)	84 (3.4)
Democratic Republic of Congo (3 projects)	414 (16.8)
Zimbabwe (2 projects)	653 (26.5)
Uganda (1 project)	52 (2.1)
India (1 project)	66 (2.7)
Myanmar (4 projects)	1184 (48.3)
History of anti-tuberculosis treatment*	
No	2232 (94.1)
Yes	139 (5.9)
Site of disease	
Smear-positive PTB (±EPTB)	158 (6.5)
Smear-negative PTB (±EPTB)	1353 (55.2)
TB meningitis	50 (2.0)
TB lymphadenitis	283 (11.6)
Other sites EPTB	139 (5.7)
EPTB site not documented	468 (19.1)
Treatment regimen	
HRZE/HR	1680 (68.5)
HRZE/HE	13 (0.5)
HRZ/HR	615 (25.1)
SHRZE/HRZE/RHE	143 (5.8)
HIV status	
Positive	935 (38.2)
Negative	578 (23.6)
Unknown	938 (38.3)

*Data not available for transferred-in children (n = 80).
PTB = pulmonary TB; EPTB = extra-pulmonary TB; TB = tuberculosis; H = isoniazid; R = rifampicin; ; Z = pyrazinamide; E = ethambutol; S = streptomycin; HIV = human immunodeficiency virus.

Table 2 Univariate analysis of risk factors associated with death during TB treatment (N = 2451)

Variable	Total n	Death n (%)	OR (95%CI)
Overall	4521	8.6 (211)	
Sex			
Male	1256	9.2 (116)	0.9 (0.6–1.1)
Female	1195	7.9 (95)	
Age group, years			
0–4	1026	10.7 (110)	0.6 (0.5–0.8)
5–15	1425	7.1 (101)	
Region			
Central Africa	1201	10.5 (126)	0.6 (0.5–0.8)
Asia	1250	6.8 (85)	
Year of enrolment			
2007	819	9.0 (74)	—
2008	825	6.7 (55)	0.7 (0.1–1.0)
2009	615	9.8 (60)	1.1 (0.8–1.6)
2010	192	11.5 (22)	1.3 (0.8–2.2)
History of anti-tuberculosis treatment			
Yes	139	14.4 (20)	0.0
No	2232	8.2 (184)	
Site of disease			
Smear-positive PTB (±EPTB)	158	5.1 (8)	—
Smear-negative PTB (±EPTB)	1223	9.61 (130)	2.0 (1.0–4.2)
TB meningitis	50	18 (9)	4.1 (1.5–11.3)
TB lymphadenitis	283	4.6 (13)	1.0 (0.4–2.2)
EPTB other site	139	8.6 (12)	1.8 (0.7–4.5)
EPTB site unspecified	468	8.3 (39)	1.7 (0.8–3.7)
HIV status			
Negative	578	5.19 (30)	
Positive	935	12.83 (12)	2.7 (1.8–4.1)
Unknown	938	6.5 (61)	1.3 (0.8–2.0)

TB = tuberculosis; OR = odds ratio; CI = confidence interval; PTB = pulmonary TB; EPTB = extra-pulmonary TB; HIV = human immunodeficiency virus.

Table 3 Anti-tuberculosis treatment outcomes by HIV status ($N = 2451$)

Anti-tuberculosis treatment outcome	HIV-positive *n* (%)	HIV-negative *n* (%)	HIV status unknown *n* (%)
Cured	35 (3.8)	41 (7.1)	31 (3.3)
Completed	679 (72.6)	402 (69.5)	718 (76.5)
Died	120 (12.9)	30 (5.7)	61 (6.5)
Failed	6 (0.6)	4 (0.7)	7 (0.8)
Default	77 (8.2)	60 (10.4)	101 (10.8)
Transfer out or altered regimen	18 (1.9)	41 (7.1)	20 (2.1)
Total	935	578	938

HIV = human immunodeficiency virus.

<5 years had increased odds of death (OR 1.7, 95%CI 1.2–2.4) compared with children aged 5–14 years, accounting for all other variables in the model. Children with tuberculous meningitis had increased odds of death compared with children with pulmonary TB (OR 2.6, 95%CI 1.0–6.8). In addition, retreatment cases tended towards a significantly higher odds of death than new cases (OR 1.7, 95%CI 0.9–2.9; Table 4).

There was significant interaction between region of residence and HIV status. In sub-Saharan Africa, the odds of death during anti-tuberculosis treatment were higher in children with unknown HIV status (OR 1.9, 95%CI 1.1–3.3) than in HIV-negative children. In Asia, there were similar odds of death in the two groups (Table 5).

Table 4 Multivariate analysis of 1464 children with known HIV status showing odds of death during anti-tuberculosis treatment

Variable	Unadjusted OR (95%CI)	Adjusted OR (95%CI)*
HIV status		
Positive	2.7 (1.8–4.1)	2.6 (1.6–4.2)
Negative	—	
Age group, years		
0–4	1.5 (1.1–2.2)	1.7 (1.2–2.5)
5–15	—	
Region		
Central Africa	1.1 (0.8–1.6)	
Asia	—	—
History of anti-tuberculosis treatment		
Yes	1.6 (1.0–2.8)	1.7 (0.9–2.9)
No	—	—
Site of disease		
PTB	—	—
TB meningitis	2.2 (1.0–4.6)	2.6 (1.0–6.8)
TB lymphadenitis	0.5 (0.3–0.9)	0.9 (0.4–1.8)
EPTB other site	0.9 (0.7–1.3)	1.5 (0.9–2.4)
Start year		
2007	—	
2008	0.5 (0.3–0.8)	0.6 (0.4–0.9)
2009	0.7 (0.5–1.1)	0.9 (0.4–1.8)
2010	1.0 (0.5–1.7)	0.8 (0.9–2.1)

*Adjusting for the clustered effect of the project, all other variables in the model.
HIV = human immunodeficiency virus; OR = odds ratio; CI = confidence interval; PTB = pulmonary TB; TB = tuberculosis; EPTB = extra-pulmonary TB.

Table 5 Odds of death following anti-tuberculosis treatment in children with unknown HIV status vs. HIV-negative children ($n = 1516$)

	HIV unknown *n* (%)	Unadjusted OR (95%CI)	Adjusted OR (95%CI)
Africa ($n = 708$)	36.8 (261)	2.1 (1.2–3.7)	1.9 (1.1–3.3)*
Asia ($n = 808$)	83.78 (677)	1.5 (0.5–4.4)	1.3 (0.4–4.2)†

*Adjusting for age, year of enrolment, site of disease and accounting for the intracluster effect.
†Adjusting for age, year of enrolment, site of disease, history of previous treatment, and accounting for intracluster effects.
HIV = human immunodeficiency virus; OR = odds ratio; CI = confidence interval.

DISCUSSION

Our study population included the largest reported community-based multinational cohort involving children with TB-HIV co-infection to date. The diversity of settings means that these data can be seen as representative of the situation in high-burden countries; comparisons were facilitated by standardisation of treatment among MSF programmes.

The overall proportion of children who died on anti-tuberculosis treatment in our cohort was 8.6%; this figure is comparable with those from observational studies in sub-Saharan Africa, where mortality ranged from 6.9% in Cape Town[12] to 17% in Malawi.[8] The main factors associated with death in our study were tuberculous meningitis, HIV infection and age <5 years. If the WHO target of zero child deaths from TB is to be reached, it will be imperative to address these high-risk groups with better prevention strategies, rapid diagnosis and effective treatment.

Our findings highlight the higher risk of death in children with TB aged <5 years than in those aged 5–15 years (10.7% vs. 7.1%). This is consistent with epidemiological studies in Brazil[13] and Botswana.[14] Further work is planned to see if this mortality disparity continues along the age gradient, i.e., between children and adults in these cohorts. There is no non-TB control group in the study, which means that the higher mortality may be attributed to age as much as TB disease.

Our study confirms the high mortality associated with tuberculous meningitis, a clinical presentation seen in young children in particular.[15,16] Most younger children with TB contract the disease from a close contact. There is good evidence that isoniazid preventive therapy can protect children from active disease.[17] Going a step further, efforts to reduce TB in the adult population, and aggressively reduce transmission by means of contact tracing and prophylaxis could also lead to a reduction in childhood TB. Transmission reduction is notoriously challenging,[18] but has proved cost-effective in high-burden settings.[19]

HIV coinfection was associated with increased risk of death during anti-tuberculosis treatment, as has been reported elsewhere.[20] Our endpoint was all-cause

mortality during anti-tuberculosis treatment, and it is probable that some of the excess mortality in this group is attributable to other HIV-related conditions. Other studies have shown that ART reduces the risk of death during anti-tuberculosis treatment in children who are HIV-positive.[21] We did not find this in our study, although very few children were documented to be receiving ART. Further analysis was not possible due to missing data on ART usage and timing of initiation. The programmes had separate HIV and TB databases, which may have contributed to the high level of missing data for these variables.

Only 6.5% (n = 158) of our study population had microbiologically confirmed TB. This represents the clinical experience of many paediatric TB programmes treating HIV-positive and -negative children. When a child is treated for 'presumed' TB, alternative pathologies (more likely in HIV-positive children) are not being treated. This is one possible explanation for the higher risk of death in HIV-positive children, i.e., these children were dying of other opportunistic infections that might have been diagnosed and treated if TB had been excluded. Rennert et al. reviewed the history of 93 HIV-positive children who died.[22] From that cohort, only 19% of children who had been receiving anti-tuberculosis treatment had evidence of TB on post-mortem examination. In our study, mortality in smear-positive children was only 5.1% compared with 9.6% in those who were smear-negative. Although the difference was not significant in our study, it has been shown elsewhere that the risk of death is greater in children smear-negative for TB whose HIV status is unknown.[8,23] New diagnostic tools, in particular those with the ability to identify resistance patterns, are crucial for early and correct diagnosis of TB in children. Trials of the Xpert® MTB/RIF platform (Cepheid, Sunnyvale, CA, USA) show promise, with sensitivity and specificity in sputum samples of respectively 80% and 95% compared with culture, providing the opportunity to diagnose pulmonary disease more rapidly and conveniently.[24] A team in South Africa has demonstrated a pick-up rate of 75.9% (95%CI 64.5–87.2) using Xpert on two induced sputum samples from children, double that diagnosed by smear microscopy.[25] Despite being a significant improvement on smear microscopy, the low numbers of organisms in expectorated sputum from children and the difficulty of obtaining sputum samples in young children limits the sensitivity of current molecular techniques and argues for better, non-sputum-based diagnostic tools to be developed for this population.

In our study, standard fixed-dose combination regimens (including rifampicin) were predominantly used. During the study period, new advice on paediatric regimens was published.[26] Our overall mortality rate of 8.6% prompts questions as to the adequacy of the treatment regimens used. Further work in monitoring changing patterns in outcome following the 2009 regimen changes is needed. The high mortality (18.0%) from tuberculous meningitis in particular argues for the inclusion of paediatric TB as a priority area for the testing of new treatments. Our findings support the WHO's call for increased use of paediatric cohorts when trialling new TB medications.

The proportion of children with documented HIV status result in this study (61.8%) is better than most reports of testing frequency in endemic areas, from 11–16% in Tanzania[27] and <30% in Botswana[14] to 63% in Thailand[7] and 69.7% in Cape Town.[28] In sub-Saharan Africa, where the pre-test probability of a positive HIV test result is higher than in Asia because of the higher prevalence of HIV, children with unknown HIV status had significantly higher odds of death than HIV-negative children. A significant proportion of these children may have had undiagnosed HIV infection and their deaths may be a result of HIV infection or untreated additional opportunistic infections. Even in these highly motivated settings, with available diagnostics and treatment, opportunities to diagnose HIV infection and prevent death from opportunistic infection seem to have been overlooked.

Analyses of routinely collected data such as ours are useful in understanding paediatric TB epidemiology in 'real world' settings, highlighting the challenges of unconfirmed diagnosis and the lack of data integration between HIV and TB services. Our findings advocate better integration of TB and HIV programmes and highlight the importance of systematic HIV testing and the institution of HIV treatment for children with TB.

However, our study also illuminates the limitations of routine data analysis. Information about significant potential confounding factors, e.g., nutritional status, severity of disease, pneumococcal vaccination status, bacille Calmette-Guérin status, drug susceptibility of the TB strains, immunological status and use of other drugs, most importantly ART drugs, was not documented or was incomplete. Our use of the TB register might have resulted in our wrongly attributing deaths to TB—particularly as time of death was not recorded—that were not in fact directly related, although this limitation applies to all groups across our study.

Our overall default rate of 9.4% did not differ significantly with HIV status, year of treatment or history of TB, suggesting that although mortality may have been under-reported the potential misclassification of death should not have been biased between HIV status groups.

CONCLUSIONS

Our analysis of routine data from programmes in Africa and Asia highlights the high risk of death from TB in children with HIV, those aged <5 years and those with TB meningitis. It also shows that there is a long way to go to achieve the WHO aim of 'zero TB

deaths in our lifetime'.[29] In addition to improved prevention and diagnostic strategies, work is needed to review whether the new dose guidelines for antituberculosis treatment are sufficient to reduce mortality, particularly for tuberculous meningitis. Testing any TB patient for HIV should be a routine part of TB care, as should instituting timely HIV treatment. Our study has shown that even in circumstances where HIV care is available not all children are tested, and they therefore do not access HIV care. Confronting the barriers to HIV testing and instituting HIV care in this vulnerable population has the potential to reduce mortality. Our study also highlights the urgent need for a reliable TB diagnostic test for children.[30] However, the challenges faced in accurately confirming a diagnosis of TB in children should not allow their plight to go unrecorded.

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RÉSUMÉ

CONTEXTE : La réalisation de la cible de zéro décès dus à la tuberculose (TB) pédiatrique de l'Organisation Mondiale de la Santé (OMS) exigera la compréhension des facteurs de risque sous-jacents à la mortalité.

OBJECTIF : Identifier les facteurs de risque de mortalité et évaluer l'impact des tests pour le virus de l'immunodéficience humaine (VIH) au cours du traitement pour la TB chez les enfants dans 13 programmes de TB-VIH de Médecins sans Frontières.

SCHÉMA : Dans une étude rétrospective de cohorte, nous avons enregistré la mortalité et analysé les facteurs de risque par les statistiques descriptives et la régression logistique. Le diagnostic a été porté sur base de l'algorithme de l'OMS et l'examen microscopique des frottis.

RÉSULTATS : Ont été traités pour TB 2451 enfants d'un âge moyen de 5,2 années (déviation standard 3,9). La moitié d'entre eux (51,0%) vivaient en Asie, le reste en Afrique sub-saharienne ; 56,0% souffraient d'une TB pulmonaire. Le diagnostic a été porté au moyen de l'examen microscopique des frottis chez 6,4% ; il y a eu 211 décès (8,6%). Parmi les 1513 enfants traités pour le VIH, 61,8% (935) étaient séropositifs ; 120 (12,8%) sont décédés par comparaison avec 30/578 (5,2%) séronégatifs. Les facteurs de risque de mortalité comportaient un test positif pour le VIH (OR 2,6 ; IC95% 1,6–4,2), un âge <5 ans (1,7 ; IC95% 1,2–2,5) et une méningite TB (2,6 ; IC95% 1,0–6,8). Le risque est plus élevé chez les enfants africains dont le statut VIH est inconnu que chez ceux confirmés comme négatifs pour le VIH (1,9 ; IC95% 1,1–3,3).

CONCLUSIONS : Les stratégies d'élimination des décès par TB chez les enfants devraient inclure le ciblage des groupes à haut risque identifiés dans cette étude, l'accentuation de la prévention de la TB, la généralisation des tests VIH et le développement d'un test rapide de diagnostic.

RESUMEN

MARCO DE REFERENCIA: El cumplimiento del objetivo de la Organización Mundial de la Salud (OMS) de la eliminación total de las muertes pediátricas por tuberculosis (TB) exigirá una buena comprensión de los factores de riesgo subyacentes de esta mortalidad.

OBJETIVO: Definir los factores de riesgo que se asocian con la mortalidad y evaluar la repercusión de la práctica de la prueba del virus de la inmunodeficiencia humana (VIH) durante el tratamiento antituberculoso de los niños, en 13 programas contra el VIH y la TB patrocinados por Médicos Sin Fronteras.

MÉTODO: En un estudio retrospectivo de cohortes, se registró la mortalidad y se examinaron los factores de riesgo mediante análisis descriptivos y de regresión logística. El diagnóstico se estableció con base en el algoritmo de la OMS y la baciloscopia del esputo.

RESULTADOS: Se trataron 2451 niños por TB cuya edad promedio fue 5,2 años (desviación estándar 3,9). La mitad de los niños residía en Asia (51,0%) y el resto en África subsahariana; el 56,0% presentó TB de localización pulmonar. El diagnóstico se estableció mediante la baciloscopia del esputo en el 6,4% de los casos; 211 niños fallecieron (8,6%). De los 1513 niños en quienes se practicó la prueba del VIH, 935 obtuvieron un resultado positivo (61,8%) y 120 de ellos fallecieron (12,8%) en comparación con 30 de los 578 niños con serología negativa (5,2%). Los factores de riesgo asociados con la mortalidad fueron la positividad de la prueba del VIH (OR 2,6; IC95% 1,6–4,2), la edad <5 años (OR 1,7; IC95% 1,2–2,5) y la meningitis tuberculosa (OR 2,6; IC95% 1,0–6,8). El riesgo de mortalidad fue más alto en los niños africanos con una situación desconocida frente al VIH que en los niños con serología negativa confirmada (OR 1,9; IC95% 1,1–3,3).

CONCLUSIÓN: Las estrategias encaminadas a la eliminación de la mortalidad por TB en los niños deben abordar los grupos de alto riesgo definidos en el presente estudio, reforzar la prevención de la TB, fomentar la práctica universal de la prueba diagnóstica del VIH e impulsar el desarrollo de pruebas diagnósticas rápidas.