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Outcomes in children treated for tuberculosis with the new dispersible fixed-dose combinations in Port Moresby

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Setting: The new child-friendly fixed dose combinations (FDCs) were introduced at Port Moresby General Hospital, Papua New Guinea, in 2016 for the first-line treatment of children (aged <15 years) with tuberculosis (TB) who weighed <25 kg.

Objective: To describe the characteristics and outcomes for children treated with the new FDCs, and to identify risk factors for unfavourable treatment outcomes.

Design: This was a retrospective cohort study of all children treated for TB with the FDCs from August 2016 to August 2017.

Results: Of 713 children included, 488 (68%) were diagnosed with pulmonary TB. Only 6 (0.8%) TB cases were bacteriologically confirmed and human immunodeficiency virus (HIV) status was known in 50%. Treatment outcomes were favourable in 425 (60%) children. Of 288 children with unfavourable outcomes, there were 242 (84%) with loss to follow-up (LTFU) and 25 (8.4%) were known to have died. Children who were severely underweight (weight-for-age Z score <–3) on presentation were at greater risk of LTFU compared to children of normal weight on multivariable analysis (aRR 1.3, 95%CI 1.0–1.6, $P < 0.05$).

Conclusion: Alternative models of care to decrease LTFU during treatment are needed, including integration with nutritional support. Improving diagnosis through microbiological confirmation of TB and HIV are major challenges to be addressed.

Tuberculosis (TB) is a major cause of morbidity and mortality among children in high-burden countries.[1] In children aged <15 years, there were an estimated 1.04 million incident cases of TB worldwide in 2016 with 253000 TB related deaths.[2] In Papua New Guinea (PNG) in 2016, the case notification rate for all forms of TB was 333 per 100000 population and children accounted for 27% of all TB case notifications,[3] higher than the global estimate of 10.6% of all TB cases, and the highest proportion of TB cases in children reported globally.[2] The vast majority of child TB cases in PNG are clinically diagnosed without bacteriological confirmation.

The burden of TB was high in the National Capital District (NCD) in 2016, with a case notification rate of 1117/100000, 21% of which occurred in children.[3] In 2016, 42.5% of TB cases in the NCD were tested for human immunodeficiency virus (HIV), compared to the national average of 35%, and 7.6% of those tested in NCD were HIV-positive.[3] Treatment success has remained low throughout the country, ranging from 55% to 65% during 2008–2016, and loss to follow-up (LTFU) is common.[3]

Young age is a consistent risk factor for mortality in children with TB. An estimated 80% of all child TB deaths globally in 2015 occurred in children aged <5 years.[4,5] Young children require higher drug dosages per weight than older children and adults to achieve adequate drug exposure. The World Health Organization (WHO) increased the recommended dosages for the first-line drugs to treat TB in young children in 2010.[6] The previously available formulations were also difficult to administer to young children to achieve these dosages, often requiring breaking multiple tablets into portions with concerns about dosing accuracy.[7] These challenges led to the development of appropriately-dosed, child-friendly, dispersible fixed-dose combinations (FDCs) consisting of rifampicin (R), isoniazid (H), pyrazinamide (Z) (RHZ) (75 mg/50 mg/150 mg) and RH (75 mg/50 mg) for the treatment of drug-susceptible TB in children weighing <25 kg; these FDCs were launched in December 2015.[6,8]

PNG was the first country in the Asia-Pacific region to introduce the new FDCs in August 2016 at Port Moresby General Hospital (PMGH, Port Moresby, PNG), situated in the NCD. We aimed to describe the characteristics and treatment outcomes for children treated with the new FDCs at PMGH and to identify the risk factors associated with unfavourable outcomes.

METHODS

Study setting

Port Moresby, the capital of PNG, has a population of 365000. PMGH is the largest hospital in PNG with 1000 beds, including 138 paediatric beds, which provides care for child TB cases mainly from the NCD and Central Province. Children treated for TB at PMGH may present as inpatients or outpatients. The approach to the diagnosis of pulmonary TB in children includes clinical evaluation, TB contact history and chest radiography. Expectorated sputum is collected if available, otherwise gastric aspirates are obtained if directed by the clinician. Two sputum samples are sent to the laboratory for examination by smear microscopy for acid-fast bacilli and Xpert® MTB/RIF assay

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(Cepheid, Sunnyvale, CA, USA). Only specimens in which rifampicin resistance is detected by Xpert are sent to the Queensland Mycobacterium Reference Laboratory (Brisbane, QLD, Australia) for mycobacterial culture and drug susceptibility testing. Laboratory investigation of extrapulmonary TB is dependent on the disease site, such as fine needle aspiration of the lymph nodes or examination of cerebrospinal fluid. Routine HIV testing is encouraged, but not always performed due to shortages of trained staff (certified training is required), the volume of patients and inconsistencies in data recording.

Study design and population

This was a retrospective cohort study of all children (aged <15 years) with presumptive drug-susceptible TB who were treated with the new FDC from TB treatment initiation at PMGH over a 1-year period (17 August 2016–16 August 2017).

Tuberculosis management in children

Treatment regimens for TB were in accordance with national guidelines.[9,10] First-line treatment included a 2-month intensive phase of daily RHZ and ethambutol (E) followed by a 4 month continuation phase of daily RH (2RHZE/4RH) for children with pulmonary TB. All forms of extrapulmonary TB were treated for 9 months, with a continuation phase of 7 months (2RHZE/7RH). Corticosteroids are routinely given for a period of 6 weeks in children with TB meningitis or pericardial TB.

Weight-based dosing of the FDCs was administered as per national guidelines (Table 1).[9,10] Following hospital discharge for inpatients or treatment initiation for outpatients, children were provided with treatment for 2 weeks and requested to attend the PMGH outpatient TB clinic for follow-up. Children who were severely underweight (weight-for-age Z score <–3) on hospital admission were requested to attend the nutritional rehabilitation clinic 2 weeks after discharge until they reached their target weight, and were followed up at the outpatient child TB clinic.

In PNG, children receiving treatment for drug-susceptible TB are supervised by family members, with no formal directly-observed treatment. Families were educated about TB treatment by the provider and given incentives, which are described below, when available. Children were followed every 1–2 months, with medication provided until the next scheduled clinic visit. At each follow-up visit, an evaluation was taken, which included weight, clinical history to determine the resolution or persistence of symptoms and an assessment of adherence to and tolerance of the medication. The number of dispersible FDC tablets to be taken each day was adjusted according to the current weight (Table 1); if a child weighed ⩾25 kg, they were changed to 'adult' FDC preparations, as per guidelines.[9,10] Repeat sputum or gastric lavage was not performed in children who had been diagnosed with bacteriologically confirmed TB. Incentives were provided when available, which included monthly transport vouchers (approximately USD2.80) and shopping vouchers (approximately USD14) at the end of the intensive phase and upon treatment completion. Additionally, the children received a gift pack of books and pencils on treatment completion.

TABLE 1 Dosing regimen by weight bands for the treatment of tuberculosis in children using the new dispersible fixed-dose combinations at Port Moresby General Hospital, Port Moresby, Papua New Guinea[8,9]

	Intensive phase		Continuation phase
	RHZ 75/50/150 mg (Dispersible tablets) *n*	Ethambutol 100 mg tablets *n*	RH 75/50 mg (Dispersible tablets) *n*
4–7.9	1	1	1
8–11.9	2	2	2
12–15.9	3	3	3
16–24.9	4	4	4
⩾25	Adult dosages and preparations		

RHZ = rifampicin, isoniazid; pyrazinamide; RH = rifampicin, isoniazid.

Data collection and analysis

The data variables collected in this study included the patients' residence, age, sex, weight, weight for age, TB site, type of TB, HIV status and treatment outcomes, which were reported according to the standard WHO and national definitions.[9,11] The data were captured in e-TB Manager (SIAPS, Arlington, VA, USA) tablets that were introduced to PMGH together with the new FDC in August 2016 by the Remote Sensing Centre (Port Morseby, PGN) and the National Health Information System (Port Morseby, PGN). After capture, the data were downloaded into an electronic database and then transferred into Microsoft Excel (Microsoft Corp, Redmond, WA, USA). The data were cross-checked with the treatment registers, the follow-up clinic registers and paediatric admission and inpatient death register books.

The data were validated and analysed in Stata v 15 (StataCorp, College Station, TX, USA). Categorical data were reported as numbers and proportions. Continuous data were reported as medians and interquartile ranges [IQR]. A modified Poisson regression using robust variance estimates was used for risk factor analysis. Associations were summarised and inferred using relative risk (RR, unadjusted and adjusted) and 95% confidence intervals (CIs).

Ethics

Ethical approval to conduct this study was obtained from the PNG Medical Research Advisory Council (Port Morseby, PNG), the PMGH (Port Moresby, PNG) and the Alfred Hospital Ethics Committee (Melbourne, VIC, Australia). As this study involved routinely collected secondary programme data, waiver of informed consent was sought and approved by the ethics committees.

RESULTS

Of 713 children who initiated treatment with the new FDCs over a 1-year period, 554 (78%) were recorded as

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TABLE 2 Clinical and demographic characteristics of children who started TB treatment using the new dispersible fixed-dose combinations at Port Moresby General Hospital, Port Morseby, Papua New Guinea, from August 2016 to August 2017

Characteristic	*n*, (%)
Total	713
Age, months	
<12	117 (16.4)
12–59	431 (60.4)
60–119	141 (19.8)
⩾120	23 (3.2)
Missing	1 (0.1)
Sex	
Male	387 (54.3)
Female	325 (45.6)
Missing	1 (0.1)
Residence	
National Capital District	554 (77.7)
Central province	144 (20.2)
Gulf province	4 (0.5)
Other	2 (0.3)
Missing	9 (1.3)
HIV status	
Uninfected	308 (43.2)
Infected	49 (6. 9)
Not known	356 (49.9)
Baseline weight, kg	
<4	4 (0.5)
4–7.9	216 (30.3)
8–11.9	229 (32.1)
12–15.9	135 (19.0)
16–24.9	119 (16.7)
Missing	10 (1.4)
TB site	
Pulmonary	488 (68.4)
Lymph node	66 (9.3)
Meningitis	47 (6.6)
Extrapulmonary, other	108 (15.1)
Missing	4 (0.6)
Case definition	
PTB bacteriologically confirmed	1 (0.1)
PTB clinically diagnosed, bacteriologically negative	34 (4.8)
PTB clinically diagnosed, not tested bacteriologically	427 (59.9)
EPTB bacteriologically confirmed	5 (0.7)
EPTB clinically diagnosed	230 (32.3)
Case definition not recorded	16 (2.2)

TB = tuberculosis; HIV = human immunodeficiency virus; PTB = pulmonary TB; EPTB = extrapulmonary TB.

residing in NCD. The demographic and clinical characteristics are summarised in Table 2. The majority (77%) of the children were aged <5 years of age, reflecting the fact that the new FDCs are only for children who weigh <25 kg (Table 1); 117 (16%) of the study population were infants aged <12 months. Pulmonary TB (68% of total cases) was the most common site and extrapulmonary TB included lymph node TB (9% of total cases), TB meningitis (7%), abdominal TB (4%), and pleural TB (2%). Less than 1% of the cohort had bacteriologically confirmed TB. HIV status was unknown in 50% of the cohort, and among 357 children with known HIV status, 13% were living with HIV.

TABLE 3 Treatment outcomes of children who commenced TB treatment using the new dispersible fixed-dose combinations at Port Moresby General Hospital, Port Moresby, Papua New Guinea

End-of-treatment outcomes	*n* (%)
Total	713 (100)
Cured	0 (0)
Treatment completed	425 (59.6)
Treatment failed	0 (0)
Died	25 (3.5)
Loss to follow-up	242 (33.9)
Not evaluated*	21 (3.0)
Not recorded	0 (0)

*Defined as a TB patient for whom no treatment outcome is assigned. This includes cases 'transferred out' to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.
TB = tuberculosis.

Table 3 shows the data on treatment outcomes. There were no children recorded as 'cured' as sputum was not collected for microscopy or culture at follow-up. There were 25 deaths. The median time from starting treatment until death was 10 days, although there a wide range [IQR 6–53]. Of the children who died, 15 (60%) had pulmonary TB and 7 (28%) had disseminated disease, 5 with TB meningitis and 2 with miliary TB. Cause of death for the remaining 3 children was unknown. Seven (28%) of the deaths were in children newly diagnosed with HIV, 9 (36%) were HIV-negative and for 9 HIV status was unknown.

One third (34%) of all children in the cohort were lost to follow-up. The characteristics associated with the outcomes of 'treatment complete' (n = 425) and 'LTFU' (n = 242) were assessed (Table 4). Children who were severely underweight (weight-for-age Z score <–3) on presentation were at significantly greater risk of LTFU compared to children of normal weight on multivariable analysis adjusting for potential confounders (adjusted RR [aRR] 1.3, 95%CI 1.0–1.6, $P < 0.05$). Multivariable analysis similarly adjusted for potential confounders did not identify any factors associated with unfavourable outcomes, defined collectively as died, LTFU, and not evaluated (data not shown). However, 93 (44%) of 212 severely underweight children (weight-for-age Z score <–3) were not tested for HIV.

DISCUSSION

This cohort study reports the outcomes of children treated with the recently developed FDCs for drug-susceptible TB. Our findings highlight the challenges of TB confirmation and retention in care that are common in many resource-poor settings. The mortality rate of 3.5% seen in our study is higher than the 2% previously reported from a cohort study of 639 children who received first-line treatment for pulmonary and extrapulmonary TB as single drug preparations in the 1980s at PMGH.[12] In comparing the outcomes of these two large PNG child TB cohorts it should be noted that the previous study was conducted prior to the HIV epidemic and included older children, while our study was limited to children weighing <25 kg. Young age and HIV infection are recognised risk factors for mortality in children treated for TB.[4] While child TB is commonly diagnosed and reported in PNG,[3] treatment outcomes, including TB-related deaths, are not well reported. Deaths due to severe TB in children can be under-represented in surveillance data because they often occur early following presentation and diagnosis, before the child can be registered

TABLE 4 Risk factors for loss to follow-up compared to treatment success in children treated with the new fixed-dose combinations at Port Moresby General Hospital, Port Moresby, Papua New Guinea

Characteristic	Treatment completion *n* (%)	Loss to follow-up *n* (%)	RR (95%CI)	aRR* (95%CI)
Total	425 (63.7)	242 (36.3%)		
Age, months (*n* = 667)				
<12	58 (13.6%)	44 (18.2%)	1.05 (0.6–1.8)	1.2 (0.7–2.2)
12–59	258 (60.7%)	151 (62.4%)	0.9 (0.5–1.5)	1.1 (0.6–1.8)
60–119	96 (22.6%)	38 (15.7%)	0.7 (0.4–1.2)	0.8 (0.5–1.5)
⩾120	13 (3.1%)	9 (3.7%)	Reference	Reference
Sex (*n* = 667)				
Male	233 (54.8%)	134 (55.4%)	Reference	Reference
Female	192 (45.2%)	108 (44.6%)	1.0 (0.8–1.2)	1.0 (0.8–1.2)
Residence (*n* = 662)				
National Capital District	339 (80.3%)	181 (75.4%)	Reference	Reference
Central province	80 (19.0%)	56 (23.3%)	1.2 (0.9–1.5)	1.1 (0.9–1.4)
Other	3 (0.7%)	3 (1.3%)	1.4 (0.6–3.2)	1.6 (0.6–2.6)
HIV status (*n* = 667)				
Uninfected	187 (44.0%)	105 (43.4%)	Reference	Reference
Infected	26 (6.1%)	14 (5.8%)	1.0 (0.6–1.5)	1.0 (0.6–1.5)
Unknown	212 (49.9%)	123 (50.8%)	1.0 (0.8–1.3)	1.1 (0.9–1.3)
Type of patient (*n* = 665)				
New	402 (94.8%)	232 (96.3%)	Reference	Reference
Previously treated	22 (5.2%)	9 (3.7%)	0.8 (0.4–1.4)	0.8 (0.4–1.4)
TB site (*n* = 666)				
Pulmonary	288 (67.8%)	171 (71.0%)	Reference	Reference
Lymph node	42 (9.9%)	20 (8.3%)	0.9 (0.6–1.3)	1.4 (0.6–2.9)
Meningitis	24 (5.6%)	17 (7.1%)	1.1 (0.8–1.6)	1.6 (0.8–3.5)
Extrapulmonary, other	71 (16.7%)	33 (13.7%)	0.98 (0.6–1.2)	1.3 (0.6–2.6)
Case Definition (*n* = 666)				
Bacteriologically confirmed	4 (0.9%)	2 (0.8%)	0.9 (0.3–2.7)	0.8 (0.2–2.7)
PTB clinically diagnosed	275 (64.7%)	167 (69.3%)	Reference	Reference
EPTB clinically diagnosed	146 (34.4%)	72 (29.9%)	0.9 (0.7–1.1)	0.8 (0.4–1.4)
Baseline weight for age, Z score (*n* = 658)				
Normal (⩾–2 Z score)	203 (48.2%)	99 (41.8%)	Reference	Reference
Underweight (<–2 to –3)	97 (23.0%)	47 (19.8%)	1.0 (0.7–1.3)	1.0 (0.7–1.3)
Severe underweight (<–3)	121 (28.7%)	91 (38.4%)	1.3 (1.1–1.6)†	1.3 (1.0–1.6)†

*Modified Poisson regression using robust variance estimates.
† $P < 0.05$.
RR = relative risk; CI = confidence interval; aRR = adjusted relative risk; HIV = human immunodeficiency virus; TB = tuberculosis; PTB = pulmonary TB; EPTB = extrapulmonary TB.

as a TB case.[13] Most of the recorded deaths occurred in inpatients within weeks following diagnosis. There is a recognised need for better data of TB-related deaths in children.[1,4,5] This study also highlights the need to improve testing coverage for HIV in children with presumptive TB.

The high proportion of LTFU described among the children in this study is similar to a previous study from PMGH,[12] where the LTFU rate was 28%. Both studies may underestimate the true mortality rate as it is likely that there were deaths among the children who were lost to follow-up. LTFU is recognised as a major contributor to the low treatment success rates that were recently reported in PNG—representing approximately 19% of all treatment outcomes in 2016 but as high as 27% in some settings.[3] LTFU and poor treatment adherence are frequent in cohorts of children treated for TB in high-burden settings.[14,15] One of the commonly perceived treatment barriers to adherence, a lack of child-friendly medicines, was not a factor in this cohort and yet retention in care remained a challenge. LFTU also occurred despite the use of incentives. However, incentives were provided inconsistently during the study period, which highlights the challenges of access and follow-up when care is centralised in a large tertiary facility. It should be noted that the LTFU rate may have been lower than reported, as the TB clinic staff may have failed to record clinic attendance in the register and accurately document treatment outcomes. Improving the quality of TB programme data is important to ensure that the data can be meaningfully used to inform accurate reporting and quality improvement activities.

Children who were severely undernourished were at highest risk of LTFU. However, when adjusting for measured potential explanatory factors, the effect size was not large, suggesting that other unmeasured factors exist. There is a known higher risk of death among children with severe malnutrition, which could explain the higher rate of LTFU. Additionally, it is possible that these children chose to attend nutritional rehabilitation services for follow-up, suggesting that coordination with nutritional services may support retention in the TB cascade of care. Finally, HIV status was unknown in a large proportion of the cohort, including children with severe malnutrition; undiagnosed HIV-infected children not being treated with antiretroviral therapy are

at risk for severe malnutrition and poor outcomes. Having sufficient numbers of trained staff to perform HIV testing in the hospital and clinic was challenging, in addition to capturing HIV testing into the electronic tablet.

This is the first study of the outcomes of children receiving FDCs in our population and can serve as a benchmark to measure future efforts to improve care. The factors associated with LTFU are likely to be multiple and complex, including behavioural, socioeconomic and health-care system related elements. Improving retention in care will require consideration of these factors when treating paediatric TB. Enabling patients to receive care closer to home by enhancing community-based treatment support may be an important factor to promote.[15]

The proportion of all bacteriologically confirmed TB in PNG is low (26% of pulmonary TB cases) and the diagnosis of pulmonary TB without sputum or of extrapulmonary TB is common.[3] The low rate of bacteriological confirmation (less than 1%) underlines the challenges of TB diagnosis in children. Additionally, for this study, accurately recording specimen collections in the electronic tablets was challenging. The consistently low diagnostic yield from smear microscopy of gastric aspirates and the lack of culture facilities has discouraged clinicians in PNG from routinely taking specimens for bacteriological confirmation of TB in children. The WHO and the PNG guidelines now recommend that children with presumptive TB have specimens tested using Xpert[9,11] and mycobacterial culture is also now available in Port Moresby (since 2017). Optimising the use of Xpert, culture and drug susceptibility testing to improve the diagnosis of child TB is important, especially in PNG, which has an increasingly high burden of drug-resistant TB.[16] Obtaining specimens from young children remains a challenge, especially in a setting where nasogastric tubes are often not available. Nonetheless, efforts to improve the laboratory detection of *Mycobacterium tuberculosis* and the spectrum of drug resistance in children are required.

This study has a number of important limitations. We did not have a control group that would allow a comparison to be made between treatment outcomes achieved using the new FDC formulations compared to the former regimen. Additionally, this was a retrospective study reliant on routinely collected programmatic data. As such, there were missing data which, despite cross checking registers, were not able to be identified, especially in regards to specimen collections for Xpert and for HIV. While this study aimed to determine risk factors for LTFU, the results may not be a true reflection of the actual risk factors as key information, notably HIV status, was missing for a large proportion of patients. Additionally, some children may have had undiagnosed drug-resistant TB. Finally, we were unable to actively trace the large proportion of the cohort lost to follow-up to determine their status and ascertain the possible reasons for not completing TB treatment at PMGH.

In conclusion, this study of a large cohort of children treated with the new FDC in PNG highlighted the need to improve retention in care, promote bacteriological confirmation of TB among children, increase access to HIV testing and improve linkages with community-based TB programmes and nutrition services.

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Contexte : La nouvelle combinaison à dose fixe adaptée aux enfants (FDC) a été introduite à l'hôpital général de Port Moresby, Papouasie Nouvelle Guinée, en 2016 pour le traitement de première ligne des enfants (agés <15 ans) atteints de tuberculose (TB) et pesant <25 kilos.
Objectif : Décrire les caractéristiques et les résultats des enfants traités par les nouvelles FDC et identifier les facteurs de risque de résultat défavorable du traitement.
Schema : Une étude rérospective de cohorte de tous les enfants traités pour TB avec ces FDC entre août 2016 et août 2017.
Resultats : De 713 enfants inclus, 488 (68%) ont eu un diagnostic de TB pulmonaire. Seulement 6 (0,8%) cas de TB ont été confirmés par bactériologie et la statut du virus de l'immunodéficience humaine (VIH) n'a été connu que pour 50% d'entre eux. Les résultats du traitement ont été favorables chez 425 (60%) enfants. Sur 288 enfants ayant eu un résultat défavorable, 242 (84%) ont été perdus de vue et 25 (8,4%) sont décédés. Les enfants atteints de malnutrition grave (score Z poids/âge <–3) à leur arrivée ont eu le risque le plus élevé de perte de vue comparés aux enfants de poids normal en analyse multivariables (RRa 1,3, IC95% 1,0–1,6 ; $P < 0,05$).
Conclusion : Des modèles de prise en charge alternative visant à réduire les pertes de vue pendant le traitement doivent être envisagés, comme par exemple une intégration avec un soutien nutritionnel. L'amélioration du diagnostic grâce à une confirmation microbiologique de la TB et du VIH sont des défis majeurs à affronter.

Marco de referencia: Las nuevas asociaciones en dosis fijas adaptadas al uso pediátrico se introdujeron en el Hospital General de Port Moresby, en Papúa Nueva Guinea, en el 2016 para el tratamiento de primera línea de los niños (<15 años) con tuberculosis (TB) con un peso <25 kg.
Objetivo: Describir las características y los desenlaces de los niños tratados con las nuevas asociaciones en dosis fijas y determinar los factores de riesgo de alcanzar desenlaces desfavorables.
Metodo: Un estudio de cohortes retrospectivo de todos los niños tratados por TB con asociaciones de dosis fijas de agosto del 2016 a agosto del 2017.
Resultados: Se incluyeron en el estudio 713 niños y se diagnosticó TB pulmonar en 488 de ellos (68%). Solo seis casos de TB contaban con confirmación bacteriológica (0,8%) y se conocía la situación frente al virus de la inmunodeficiencia humana en el 50% de los casos. Cuatrocientos veinticinco niños alcanzaron desenlaces terapéuticos favorables (60%). De los 288 niños con desenlace desfavorable, 242 fueron pérdidas durante el seguimiento (84%) y se supo que 25 niños habían fallecido (8,4%). Según el análisis multivariante, los niños con insuficiencia ponderal grave (escala Z del peso para la edad <–3) en la primera consulta corrían un mayor riesgo de pérdida durante el seguimiento que los niños con peso normal (riesgo relativo ajustado: 1,3, IC95% 1,0–1,6 ; $P < 0,05$).
Conclusion: Es necesario considerar la posibilidad de utilizar otros modelos de atención que contribuyan a disminuir el riesgo de pérdida durante el seguimiento, incluida la integración con el apoyo nutricional. Los principales desafíos que deben abordarse son mejorar el diagnóstico de la tuberculosis con la confirmación bacteriológica y de la infección por el VIH.

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