



Childhood tuberculosis in Mauritania, 2010–2015: diagnosis and outcomes in Nouakchott and the rest of the country

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Setting: The National Tuberculosis Programme, Mauritania.

Objective: To compare the diagnosis and treatment outcomes of childhood tuberculosis (TB) cases (aged <15 years) registered between 2010 and 2015 inside and outside Nouakchott, the capital city.

Design: This was a retrospective comparative cohort study.

Results: A total of 948 children with TB were registered. The registration rate was 10 times higher in Nouakchott. The proportion of children among all TB cases was higher inside than outside Nouakchott (7.5% vs. 4.6%, $P < 0.01$). Under-fives represented 225 (24%) of all childhood TB cases, of whom 204 (91%) were registered in Nouakchott. Extra-pulmonary TB was more common in Nouakchott, while smear-negative TB was less common. Treatment success was similar inside and outside Nouakchott (national rate 61%). The principal unsuccessful outcomes were loss to follow-up outside Nouakchott (21% vs. 11%, $P < 0.01$) while transfers out were more common in the city (25% vs. 14%, $P = 0.01$). Being aged <5 years (OR 1.2, 95%CI 1.1–1.5) was associated with an unsuccessful outcome.

Conclusion: This study indicates problems in the diagnosis and treatment of childhood TB in Mauritania, especially outside the city of Nouakchott. We suggest strengthening clinical diagnosis and management, improving communications between TB treatment centres and health services and pressing the TB world to develop more accurate and easy-to-use diagnostic tools for children.

The global burden of tuberculosis (TB) remains immense.¹ According to the World Health Organization (WHO), there were an estimated 10.4 million new TB patients in 2015 and 1.4 million deaths from the disease.² For the same year, the WHO estimated that approximately one million children (aged 0–14 years) developed TB, of whom 20% died.² With 31% of all estimated childhood TB cases, Africa has the world's second highest burden of TB among this population. Children, especially those aged under 5 years, are the most vulnerable, as they develop more severe forms of the disease.^{3–5} This population, however, usually receives less attention from national TB programmes (NTPs). One of the main reasons for this is that children with TB are thought to be less contagious than adults, due to their paucibacillary sputum.⁶ At the same time there are particular difficulties in the diagnosis and management of childhood TB, reflected in

the poor notification of cases.^{7,8} These difficulties include a lack of good diagnostic tools for use in children; smear microscopy is less sensitive than culture, and requires sputum specimens that children, especially under-fives, have difficulty producing.⁹ More sophisticated methods of diagnosis, such as gastric lavage, X-ray or Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA), are only available in urban centres, if at all. Furthermore, medical staff may be inadequately trained to properly recognise and diagnose TB.

In 2016, the WHO launched its End TB strategy, with targets to reduce TB incidence and related deaths by respectively 90% and 95% by 2035. The first pillar of this strategy is to focus on early diagnosis, treatment and prevention for all TB patients, including children.¹⁰

Rates of reported childhood TB vary in Africa, reflecting the difficulties with diagnosis in this population. In one study from southern Ethiopia, children with TB accounted for 13% of all TB cases, while in another, from Cotonou, Benin, they represented only 4.5%.^{11,12} Recently, in Lagos, Nigeria, the proportion of children notified with TB was 6.8%, but was slowly increasing.¹³

Mauritania, in West Africa, notifies about 2500 TB cases annually, with a notification rate of around 60 per 100000 population,² of whom approximately 6% are children. This proportion is lower than the WHO estimate of 10%.² This gap is worrying, as there is no information in the country on the management of childhood TB, particularly regarding diagnosis and outcomes. There is also a large difference in resources available for TB diagnosis between the capital city, Nouakchott, and other parts of the country, which may affect the childhood TB notification rate and the outcomes of tuberculosis treatment.

Given these gaps in knowledge, the aim of the present study was to compare the diagnosis, notification and treatment outcomes of childhood TB between the capital city and the rest of Mauritania. Specifically, we compared, among registered childhood TB cases from 2010–2015 for both regions, 1) the trend of TB notification rates, 2) the annual proportion of childhood TB among all TB cases, 3) the demographic and clinical characteristics of children with TB, and 4) the treatment outcomes.

METHOD

Study design

This was a retrospective cohort study using routinely collected programme data.

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Setting

General setting

Mauritania is a West African country with an area of approximately 1 000 000 km², of which 70% is desert. According to the last census (2013), 44% of the total population of 3 500 000 were children aged <15 years.¹⁴ Overall, the country is divided into 15 administrative regions, of which the capital city, Nouakchott, covers three. As most of the central and northern part of the country is made up of desert, the majority of the population lives along the coast or in the south-eastern part of the country; 27% live in Nouakchott.¹⁵ Mauritania is a lower middle-income country with a per capita gross national income estimated at US\$1270 in 2014.¹⁶ There were 133 000 live births registered in the country in 2013; the under-five mortality rate remains high, at 90/1000 live births.¹⁷ In 2012, the prevalence of human immunodeficiency virus (HIV) infection among adults was 0.4%.¹⁸

Mauritania National Tuberculosis Programme

The Mauritania NTP comes under the Ministry of Health, with three levels of decentralisation: central administration, intermediate coordination and peripheral health facilities. Since 1998, the NTP has instituted the DOTS strategy and followed the recommendations of the WHO and the International Union Against Tuberculosis and Lung Disease (The Union) for the diagnosis, treatment and prevention of TB. At the peripheral level, there are 58 centres for diagnosis and treatment (CDT) for TB, which are integrated into the general health facilities and serve the whole country. Four CDT are located in regional hospitals, and the others in health centres.

The NTP guide used by health workers for TB management in the CDTs was published in 2004.¹⁹ For patients with symptoms and signs of TB, the diagnosis is confirmed using microscopy with Ziehl-Neelsen staining; sputum culture is only available in the national laboratory, in Nouakchott. Xpert tests are not routinely performed in the public sector. Sputum smear microscopy, culture and anti-tuberculosis drugs are provided free of charge. For patients diagnosed with TB, HIV testing and active contact tracing are not routinely performed. Anti-tuberculosis drugs are available only in public health facilities and not in private pharmacies. Isoniazid (INH) preventive therapy (IPT) had not been implemented in the country as of 2016. Bacille Calmette-Guérin (BCG) vaccination is recommended at birth or within the first month; national BCG coverage was 93% in 2014.²⁰

Management of childhood tuberculosis in the National Tuberculosis Programme

Screening for TB in children is recommended if children: 1) are aged <5 years and are in contact with an adult smear-positive case; 2) have severe malnutrition and do not respond to therapeutic feeding; 3) have symptoms suggestive of TB, especially cough, and do not respond to treatment with broad spectrum antibiotics; or 4) are infected by HIV.

Children are usually investigated in any clinic or hospital where there is a medical doctor. A diagnosis of

TB in children is confirmed through sputum smear examination wherever possible. Other investigations needed for diagnosis when sputum examination is negative or cannot be performed, such as X-ray or the tuberculin skin test, have to be paid for by the parents and are mostly performed in Nouakchott. Gastric lavage is occasionally performed in children aged <7 years, but only in two hospitals in the capital.

Given the difficulties in obtaining satisfactory sputum samples from children, especially the under-fives, TB diagnosis is usually based on clinical signs and symptoms, especially outside the capital. Although there is an entire chapter in the NTP guide dedicated to childhood TB management,¹⁹ it does not contain a clear algorithm for TB diagnosis in children, and, as mentioned, it has not been updated since 2004.¹⁹

All children diagnosed with TB are referred to the CDT for treatment. A new TB case is treated with a 6-month regimen comprising 2 months of rifampicin (R, RMP), INH (H) and pyrazinamide (Z) in the initial phase followed by a 4-month continuation phase of RMP and INH (2RHZ/4RH).

Under-fives in close contact with smear-positive pulmonary TB cases should be investigated according to NTP recommendations. Those who are not diagnosed with TB should be treated with IPT for 9 months. IPT is not routinely performed in most CDTs within the NTP, however.

Study population

All children (aged <15 years) diagnosed with TB and registered by the NTP between January 2010 and December 2015 were included in the study.

Data variables

The data variables for this study were the estimated population size, the number of cases of all forms of TB, regardless of the age of the patients, demographics (age, sex), home (in or outside Nouakchott), TB category and type, HIV status and treatment outcomes. The categories, types and treatment outcomes of TB cases are defined in Table 1.²¹

Individual data were extracted from the national TB reference file (Excel, Microsoft Corp, Redmond, WA, USA) and single-entered into an EpiData entry software form (v. 2.0.7.22, EpiData Association, Odense, Denmark). The data were cross-checked with the TB registers in the CDT. The TB registers and the national reference file were validated twice annually by TB supervisors.

Data analysis

Data were exported into R software (v3.2.1, R Foundation for Statistical Computing, Vienna, Austria) for analysis. Frequencies and percentages were calculated for categorical variables. The χ^2 and Wilcoxon tests were used to compare percentages and medians, respectively. Factors associated with an unsuccessful outcome were reported using risk ratios (RR), and 95% confidence intervals (CI). The level of significance was $P < 0.05$.

Ethics

Permission to carry out the study was obtained from the Mauritania NTP. As there is no ethics committee in

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TABLE 1 TB: definitions of terms used

Term	Definitions ²¹
New case	Patient never treated for TB or treated for <1 month
Retreatment case	Patient previously treated for ≥ 1 month with anti-tuberculosis drugs
Smear-positive TB	Presence of acid-fast bacilli in ≥ 1 sputum smear specimens at the start of treatment
Smear-negative TB	Patient who fulfils the following criteria: 1) presence of presumptive symptoms of TB; 2) negative result on sputum smears; 3) absence of response to broad-spectrum antibiotics after 10 days; 4) presence of radiographic abnormalities consistent with active TB; 5) decision to treat with a full course of anti-tuberculosis therapy
Smear not done	Patient diagnosed with TB for whom sputum smear testing was not performed
EPTB	Involvement of organs other than the lungs
Definitions of tuberculosis treatment outcomes	
Cure	TB patient smear-positive at the beginning of treatment with a negative smear and/or culture result in the last month of treatment and on at least one previous occasion
Treatment completion	Patient who completed treatment but did not fulfil the criteria required to be declared cured
Failure	Patient whose sputum smear or culture is positive at 5 months or later during the course of treatment
Death	Patient died during the course of treatment, regardless of the cause of the death
LTFU	Patient whose treatment was interrupted for 2 consecutive months or more during the course of treatment
Transferred out	Patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown
Treatment success	Cure, completion
Unsuccessful outcome	Failure, death, LTFU, transfer out

TB = tuberculosis; EPTB = extra-pulmonary TB; LTFU = loss to follow-up.

the country, local ethics approval was not obtained. The study fulfilled the exemption criteria set by the Ethics Review Board (ERB) of Médecins Sans Frontières (MSF, Geneva, Switzerland) for a posteriori analyses of routinely collected data, and did not require MSF ERB review. The study was conducted with permission from the medical director of the MSF Operational Centre (Brussels, Belgium). The study was also approved by the Ethics Advisory Group of The Union. As this was a record review study, informed patient consent was not required.

RESULTS

In total, 948 children were notified with TB at national level between 2010 and 2015. These represented respectively 8% and 4% of all cases diagnosed with TB in Nouakchott and outside Nouakchott. In the same period, the number of adults diagnosed with TB was 1.9 times higher in Nouakchott ($n = 8807$) compared to the rest of the country ($n = 4588$). The trends of childhood TB notification rates inside and outside Nouakchott are shown in Figure 1. Over time the notification rate was consistently 10-fold higher in Nouakchott than in the rest of the country.

A comparison of the demographic and clinical characteristics of the childhood TB cases inside and outside Nouakchott is presented in Table 2. Children aged <5 years represented 225 (24%) of the total, of whom 204 (91%) were registered in Nouakchott. The median ages of the children were respectively 9 years (± 8) and 11 years (± 6) inside and outside Nouakchott. Almost all were new cases. Among those diagnosed with smear-positive TB, 78% were aged 5–14 years and 22% were aged <5 years. While extra-pulmonary TB (EPTB) cases were more frequent in Nouakchott, children with smear-negative TB or with smear not done were more common in the countryside. The proportion of children among all TB cases was significantly higher in Nouakchott than in the rest of the country (7.5% vs. 4.6%, $P < 0.01$). No HIV testing was undertaken among children diagnosed with TB during the study period.

The treatment outcomes for all childhood TB cases are presented in Table 3 and Figure 2. Overall, the success rate was 61%;

there was no significant difference in treatment success between Nouakchott and the rest of the country. Loss to follow-up (LTFU) was significantly higher outside Nouakchott, while transfer out was reported more often in Nouakchott. Factors associated with unsuccessful outcome are shown in Table 4. Only the group of under-fives was associated with unsuccessful treatment.

DISCUSSION

This is the first study to assess TB management among children in Mauritania. It compared the diagnosis and treatment outcomes in children diagnosed with TB between Nouakchott and the rest of the country between 2010 and 2015. The main findings were that the overall childhood TB notification rate was approximately 10 times higher in Nouakchott than in the countryside, and that 90% of the under-fives with TB were diagnosed in the capital city. Surprisingly, smear-negative pulmonary TB or smear not done, which usually require medical advice for diagnosis, were more common outside Nouakchott, where resources and medical staff are limited. Approximately two thirds of all children with TB were

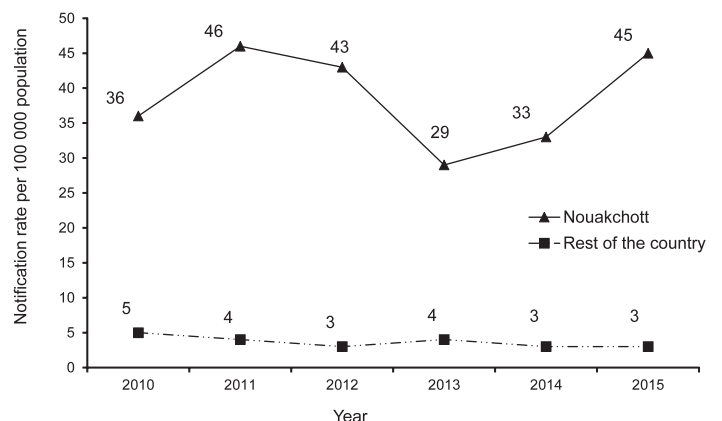


FIGURE 1 Annual childhood tuberculosis notification rate in Nouakchott and the rest of the country, Mauritania, 2010–2015.

TABLE 2 Comparison of demographic and clinical characteristics of childhood TB cases between the capital city, Nouakchott, and the rest of the country, Mauritania, 2010–2015

Characteristics	Nouakchott <i>n</i> (%)	Rest of the country <i>n</i> (%)	<i>P</i> value
All cases	9539	4804	
Children	732	216	
Age group, years			
0–4	204 (28)	21 (10)	<0.001
5–14	528 (73)	195 (90)	
Median age, years [±IQR]	9 (±8)	11 (±6)	
Sex			
Male	398 (54)	111 (51)	NS
Female	334 (46)	105 (49)	
Category of TB			
New case	725 (99)	215 (99)	—
Retreatment case	5 (1)	1 (1)	
Type of TB			
Smear-positive	276 (37)	75 (35)	NS
Smear-negative or smear not performed	138 (19)	66 (30)	<0.001
Extra-pulmonary	318 (44)	75 (35)	0.02

TB = tuberculosis; IQR = interquartile range; NS = non-significant.

TABLE 3 Treatment outcomes of childhood TB in the capital city, Nouakchott, and the rest of the country, Mauritania, 2010–2015

Outcome	Nouakchott <i>n</i> (%)	Rest of the country <i>n</i> (%)	<i>P</i> value
Total evaluated	732	216	
Successful outcome	437 (60)	140 (65)	NS
Cure*	51 (7)	30 (14)	0.01
Treatment completion†	386 (53)	110 (51)	NS
Unsuccessful outcome	295 (40)	76 (35)	NS
Failure	0	0	—
Death	28 (4)	0	0.01
LTFU	80 (11)	45 (21)	<0.001
Transferred out	187 (25)	31 (14)	0.01

* Only assessed in smear-positive TB patients.

† Assessed for patients who were smear-negative or smear not done, EPTB or smear-positive TB patients who did not undergo their last sputum follow-up examination but completed their treatment.

TB = tuberculosis; NS = non-significant; LTFU = loss to follow-up; EPTB = extra-pulmonary TB.

successfully treated in both Nouakchott and the rest of the country, but this rate did not improve over 6 years. Unsuccessful outcomes were mainly due to LTFU or transfer out, for which outcomes were unknown after transfer.

These findings are important because they confirm our impression that diagnosis of childhood TB is much worse in the countryside where physicians, mainly general physicians, make their diagnoses mostly on clinical grounds, as they do not have access to other diagnostic tools. The lack of improvement in the rates of notification and outcomes over time also indicates a lack of new approaches to address these issues during the study period.

The strengths of this study are that it included all children notified with TB countrywide over a 6-year period. Once TB has been diagnosed, hospitals without a CDT must refer patients to the NTP for treatment; this reduces the risk of underreporting. Furthermore, our data were validated at the CDTs and at regional level at least twice annually. The study also followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.²²

Limitations of the study are related to its retrospective nature, with some missing data, such as the site of EPTB, which would have allowed a better understanding of this form of the disease in Mauritania. The validation process, however, minimised some of

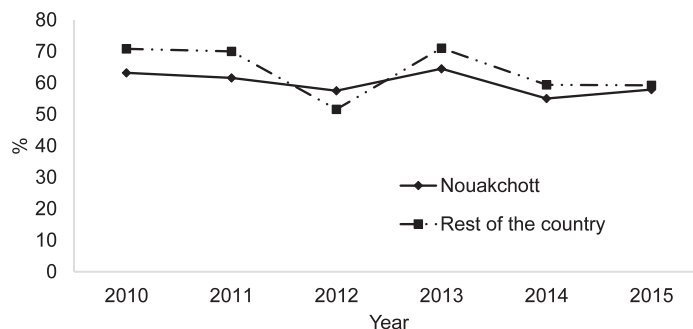
**FIGURE 2** Treatment success rate trends in Nouakchott and the rest of the country, Mauritania, 2010–2015.

TABLE 4 Factors associated with an unsuccessful treatment outcome among childhood TB cases in Mauritania, 2010–2015

Characteristics	Unsuccessful outcome <i>n/N*</i> (%)	Crude RR (95%CI)	<i>P</i> value
Region			
Nouakchott	295/732 (40)		
Rest of the country	76/216 (35)	1.1 (0.9–1.4)	NS
Age group, years			
5–14	267/723 (37)		
0–4	104/225 (46)	1.2 (1.1–1.5)	0.02
Sex			
Male	209/509 (41)		
Female	162/439 (37)	1.1 (0.9–1.3)	NS
Category of TB			
New cases	368/942 (39)		
Retreatment cases	3/6 (50)	0.8 (0.3–2.1)	NS
Type of TB			
Smear-positive	136/351 (39)		
Smear-negative or smear not performed	70/204 (34)	1.2 (0.9–1.4)	NS
EPTB	162/393 (41)	0.9 (0.7–1.1)	NS

**N* = total number of patients registered with the characteristic; *n* = unsuccessfully treated patients.

TB = tuberculosis; RR = risk ratio; CI = confidence interval; NS = non-significant; EPTB = extra-pulmonary TB.

these limitations. Despite strong WHO recommendations to investigate the HIV status of all TB patients,²³ HIV testing was seldom performed, perhaps because of a lack of collaboration between the two programmes and an overall low prevalence of HIV in the country.¹⁸

The notification rate of childhood TB in Mauritania was lower than in WHO estimates;² this appears to be due mainly to underdiagnosis, mostly in the countryside. Diagnosing TB in children is more challenging than in adults because of difficulties identifying relevant symptoms of the disease and obtaining adequate specimens, especially in under-fives. Without up-to-date guidelines and training, and additional diagnostic tools, rural physicians will not find more childhood TB cases.^{7–9} Additional diagnostic procedures such as gastric lavage and X-rays have to be paid for by the patients, and this could also be a limitation. Another possible reason for the low notification rate is that children who are symptomatic may not reach the health services at all but are taken to traditional healers, as is commonly observed in Africa.²⁴ Furthermore, the lack of investigation of under-fives in close contact with an adult smear-positive TB case probably contributed to the low diagnosis and notification of these cases.

The higher notification rate in Nouakchott was not surprising, considering the availability of more competent and specialised human resources (paediatricians) and diagnostic tools in the capital city. However, it is possible that children with TB symptoms from the rest of the country are referred or are brought by parents to consult paediatricians in the capital for diagnostic investigation. Once diagnosed and started on treatment they may return home, thus reflecting the higher rate of transfers out.

Surprisingly, TB cases with sputum smear-negative results or smear not done were less frequent in Nouakchott than in the rest of the country. We cannot explain this finding, but suggest that physicians may have been reluctant to start treatment without bacteriological confirmation. The outdated 2004 NTP guide does not provide guidance in diagnosis of TB, and it should be updated in line with international recommendations.^{4,5}

Overall, the childhood treatment success rate was similar in Nouakchott and in the rest of Mauritania, but was lower than in adults (61% vs. 70%), and also lower than in other settings in Africa (72–85%).^{12,25–27} The LTFU rate of 13% was similar to that in other countries (e.g., 18% in Togo), and reflects the fragmentation of diagnosis and treatment in Mauritania.

This study has several operational implications. After a number of years with no real improvement in diagnosis or treatment outcomes, Mauritania needs to address its TB management for children. A first step would be to develop a new national TB guide with clear diagnostic algorithms that can be taught and widely disseminated to all health workers who manage sick children. Second, the NTP should work toward covering the diagnostic costs for presumptive childhood TB cases requiring X-rays and gastric lavage, and should consider investing in Xpert to improve diagnostic sensitivity.²⁸ Third, better collaboration between the TB and HIV programmes is needed to implement regular HIV testing for all presumptive and diagnosed TB patients. Fourth, communications between paediatricians, hospitals, CDTs and health centres should be improved to reduce the number of children registered as transfers out who are eventually recorded as LTFU. Finally, further investigations are needed to better understand the real reasons for the high LTFU rate in the country.

In conclusion, this study highlights weaknesses in the Mauritanian NTP in the diagnosis of childhood TB, especially in those aged <5 years and living outside the capital city. Programmatic changes to improve the diagnosis and outcomes of this vulnerable population are suggested.

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Contexte : Programme National Tuberculose, Mauritanie.

Objectif : Comparer les résultats en termes de diagnostic et de traitement des cas de tuberculose (TB) de l'enfant (<15 ans) enregistrés entre 2010 et 2015 dans la capitale, Nouakchott, et à l'extérieur de la capitale.

Schéma : Une étude rétrospective comparative de cohorte.

Résultats : Au total, 948 enfants atteints de TB ont été enregistrés. Le taux d'enregistrement a été 10 fois plus élevé à Nouakchott. La proportion des enfants parmi tous les cas de TB a été plus élevée à Nouakchott qu'à l'extérieur (7,5% contre 4,6% ; $P < 0,01$). Les enfants âgés de <5 ans ont constitué 225 cas, soit 24% de tous les cas de TB de l'enfant, dont 204 (91%) ont été enregistrés à Nouakchott. La TB extra-pulmonaire a été plus fréquente à Nouakchott, tandis que la TB à frottis négatif a été moins fréquente.

Le taux de réussite du traitement a été similaire à Nouakchott et à l'extérieur (taux national de 61%). Les principaux résultats défavorables ont été les pertes de vue à l'extérieur de Nouakchott (21% vs. 11% ; $P < 0,01$), tandis que les transferts ont été plus fréquents dans la capitale (25% vs. 14% ; $P = 0,01$). L'âge inférieur à 5 ans a été associé à un résultat défavorable (OR 1,2 ; IC95% 1,1–1,5).

Conclusion : Cette étude a mis en évidence les problèmes de diagnostic et de traitement de la TB de l'enfant en Mauritanie, surtout hors de Nouakchott. Nous suggérons de renforcer le diagnostic clinique et la prise en charge, d'améliorer la communication entre les centres de traitement de la TB et les services de santé et de pousser le milieu de la TB à élaborer des outils de diagnostic plus précis et faciles à utiliser pour les enfants.

Marco de referencia: El Programa Nacional contra la Tuberculosis de Mauritania.

Objetivo: Comparar los diagnósticos y los desenlaces terapéuticos de los casos de TB en los niños (<15 años de edad) registrados del 2010 al 2015 en la capital Nouakchot y fuera de esta ciudad.

Método: Estudio de cohortes retrospectivo comparativo.

Resultados: En general, se registraron 948 niños con TB. La tasa de registro fue 10 veces más alta en Nouakchot. La proporción de niños en todos los casos de TB fue más alta en Nouakchot que fuera de la capital (7,5% contra 4,6%; $P < 0,01$). De todos los casos de TB en la infancia, 225 fueron niños <5 años de edad (24%), de los cuales 204 se registraron en Nouakchot (9%). La TB extrapulmonar fue más frecuente en la capital y se observó allí una menor frecuencia de casos con baciloscopia negativa. La tasa de éxito

terapéutico fue equivalente en Nouakchot y fuera de la ciudad (tasa nacional 61%). Fuera de la capital, el principal desenlace desfavorable fue la pérdida durante el seguimiento (21% contra 11%; $P < 0,01$) y en Nouakchot fueron las transferencias a otros centros (25% contra 14%; $P = 0,01$). La edad <5 años se asoció con un desenlace desfavorable (cociente de posibilidades 1,2; IC95% 1,1–1,5).

Conclusión: El presente estudio pone de manifiesto los problemas del diagnóstico y el tratamiento de la TB en Mauritania, sobre todo fuera de la capital Nouakchot. Se recomienda fortalecer el diagnóstico clínico y el tratamiento, con una mejor comunicación entre los centros de tratamiento de la TB y los servicios de salud y urgir en el mundo de la TB el desarrollo de medios diagnósticos dirigidos a los niños que sean más exactos y de utilización sencilla.