Tuberculosis in South and Central Africa

Understanding epidemiology - Improving diagnosis and management

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Chapter 2

Childhood tuberculosis in Lambaréné, Gabon: tuberculosis control in its infancy?

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ABSTRACT

Central Africa is a region highly affected by the tuberculosis (TB) pandemic; however, data on local epidemiology are scarce. In the quest for gearing up towards tailored interventions, assessment of local baseline situations is mandatory. We conducted a retrospective study of 62 children registered in the TB register of a hospital in Lambaréné, Gabon. The evaluation revealed a discrepancy between the TB burden and the commitment to control TB. Extrapolation of the incidence suggests an unexpectedly high childhood TB burden, assuming that the official overall TB incidence is an underestimate of the true TB burden in Gabon.
INTRODUCTION

Tuberculosis (TB), in the face of the human immunodeficiency virus (HIV) co-pandemic, is a major cause of morbidity and mortality worldwide, with sub-Saharan Africa among the worst affected regions [1, 2]. During the past two decades numerous international funding agencies have been founded to halt the growing TB epidemic. The “DOTS Strategy” has emerged as a successful approach to slow down and reverse the increasing incidence of TB and is currently widely implemented—or at least its implementation is attempted. The five elements of the DOTS strategy are (1) political commitment with increased and sustained financing, (2) case detection through quality-assured bacteriology, (3) standardized treatment with supervision and patient support, (4) an effective drug supply and management system and (5) a monitoring and evaluation system as well as impact measurement [3]. The Central African country of Gabon did not qualify for support by international donors and programs because of its high per capita income due to its commodities (predominantly petrol). Consequently, the national TB programme (NTP) in Gabon is entirely financed by the state. In 2010, TB incidence in Gabon was estimated to be 553 per 100,000 general population with a case detection rate of 42 % [4]. The adult HIV infection rate is reported to be around 5.2 % [5], and cases of multidrug resistant (MDR) and extensively drug-resistant (XDR) TB are emerging [6]. Despite the alarming incidence of TB and the growing threat of drug-resistant TB, systematic data on local epidemiology and microbiology are lacking for Gabon as well as for most other countries of the Central African region.

The paediatric TB disease burden is a useful indicator of current transmission within the community as it is predominantly caused by primary disease and not by reactivation. Childhood TB is estimated to account for up to 25–40 % in some high TB burden settings [7]. Management of childhood TB constitutes a major challenge within TB control programmes as case ascertainment is difficult due to less specific clinical presentation, paucibacillary TB and complicated sample collection.

Reliable data on the ongoing TB epidemic in Gabon are not available. Therefore, we have described childhood TB in one location (Lambaréné) in order to estimate its burden in Gabon and to draw conclusions on requirements to improve general and childhood TB control.

METHODS

This was a retrospective study in which we evaluated the patient records of pediatric patients registered between 1 October 2009 and 30 September 2010 in the
paediatric TB register of the Albert Schweitzer Hospital (HAS) in Lambaréné, Gabon. Lambaréné is a semi-urban setting with 25,000 inhabitants. In Lambaréné, TB patients are treated in the HAS, the public hospital or the public HIV/TB clinic. The HAS has no designated TB department, and TB patients are generally treated within the internal medicine and paediatric wards and the respective outpatient clinics. As TB drugs supplied by the NTP can be subject to interruptions, the HAS independently procures first-line TB drugs which are distributed to the hospital’s patients free of cost. The paediatric ward has 34 beds, and approximately 2,500 and 6,000 patients up to the age of 15 years are treated in the in- and outpatient clinic annually.

Predefined data (data on demography, medical history, clinical presentation, diagnostics, treatment and outcome) were extracted from patient records and the paediatric TB register and imported into a purpose-built database. Healthy patients who were registered due to contact history but without clinical signs or symptoms of TB were excluded from the analysis. Pulmonary TB (PTB) was defined as pulmonary involvement with or without concurrent extrapulmonary manifestations; extra-pulmonary TB (EPTB) was defined as TB without pulmonary involvement. For children aged <5 years, body weight was evaluated according to the local weight-for-age growth charts comprising three weight categories (MPE: malnutrition protéino-énergétique): normal nutrition and moderate and severe malnutrition. For children aged ≥5 years, weight-for-age percentiles from the Centers for Disease Control and Prevention (Atlanta, GA) were used because local growth charts for this age group were not available. For the descriptive presentation of the data, data ranges, means, medians and ratios were calculated using Microsoft Office Excel 2007 (Microsoft, Redwood, WA). To estimate the extent of the paediatric TB burden, ratios were calculated using the number of cases, official demographic data [8] and TB incidence estimates by the WHO [4]. Ethical approval was not needed as only anonymized retrospective data from routine patient care were analyzed; this decision was officially confirmed by the Institutional Review Board.

RESULTS

During the 1-year period from October 2009 and September 2010 66 children were registered in the paediatric ward’s TB registry. Four children were excluded from the retrospective evaluation because they were contact persons without signs and symptoms of TB disease. A total of 62 children were evaluated in the final analysis, but for 12 of these (19 %) patient records had been lost and only data from the registry were available.
The age of the 62 children ranged from 3 months to 14 years: 38 (61 %) were <5 years old and ten (16 %) were >10 years old. In the group of children <5 years old the median age was 21 months; in those aged >5 years the median age was 9 years. Of the 62 children, 25 (40 %) were female; in comparison, one-third of children in the group of <5 years old (n = 11, 29 %) were female and two-thirds of children in the group of >5 years (n = 14, 61 %) were female.

In all but one patient (n = 61) data were available on the type of TB. Fifty-two (85 %) children suffered from PTB and nine (15 %) had EPTB. This ratio was similar in the patient groups of <5 and >5 years old, with 32/6 (84/16 %) and 20/3 (87/13 %) PTB/EPTB cases, respectively. Of these 61 patients, 45 (74 %) had pulmonary involvement only (including one patient with nodular chest X-ray aspect), seven (11 %) had lymphadenopathy only, five (8 %) had pulmonary involvement with lymphadenopathy and two (3 %) had pleural effusion with pulmonary TB and bone TB, respectively.

Information on HIV status was only available for 12 of the 62 (19 %) patients; one child (aged 4 months) was diagnosed with HIV infection.

Of the 62 patients, information on symptoms upon admission was available for 44 (71 %). Respiratory symptoms (cough and dyspnoea) were the most commonly documented symptoms, followed by fever, weight loss and lymphadenopathy (n = 29, 20, 16, 13, respectively). Twenty-six patients had cough, four had dyspnoea and one had haemoptysis. Lymphadenopathy was most commonly cervical, followed by intra-abdominal and axillary locations. Body weight prior to treatment start was documented in 50 of the 62 children (81 %). Data for the age group <5 years (n = 30) revealed low body weight corresponding to local moderate and severe malnutrition in eight (27 %) and ten (33 %) patients, respectively. In the >5 year-old, only three of 20 (15 %) patients were below the 5th percentile.

Pulmonary X-ray documentation was available for 37 of the 62 patients (60 %); of these, the documentation for 35 children (95 %) contained pathological findings. The result of a tuberculin skin test was documented for 38 of the 62 children (61 %), of whom 26 (68 %) had a positive reaction of >10 mm. A positive microscopic pharynx secretion or sputum result was documented for three of the 62 children (5 %) (ages 16 months, 9 and 12 years, respectively). Gastric lavage was not performed.

A history of TB contact was documented in 30 of the 62 children (48 %). Most often the index patient was the mother, followed by the father, sister or brother. Residence was documented for 60 children (97 %), of whom 32 (53 %) lived within the town limits of Lambaréné.

In Gabon BCG vaccination is routinely given at birth and documented in the child’s health booklet which is kept with the family. No data on BCG immunization were available for this retrospective evaluation. However, in 2010, WHO reported that coverage was 68 % [9].
All children received exclusively the first-line anti-TB drugs of rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E) and started treatment while hospitalized. Of the 62 children, 55 (89%) were initially treated with a triple regimen of RHZ, while seven (11%) received RHZE during the initiation phase. During the continuation phase, RH were the drugs prescribed. Directly observed therapy was not practiced. Of the 62 children, 36 (58%) were classified as having completed treatment, 17 (27%) were lost to follow-up, three (5%) were transferred to the internal medicine ward or to another hospital and two (3%) died; for the remaining four patients (6%), no information on treatment outcome was available due to loss of patient records and absence of outcome entry in the register. The two children who died had received 9 and 14 days of RHZ, respectively; both were 4 months old, and one was HIV positive. Of the 17 children lost to follow-up, ten (59%) did not reside in Lambaréné. Information on weight before and after treatment was available for 34 children: 31 (91%) gained weight and 21 (62%) increased their weight category (MPE or percentile).

DISCUSSION

The aim of this evaluation was to identify the most urgent requirements for improving management of childhood TB and general TB control in Gabon. The following discussion will focus on the most relevant findings revealed by this study.

Firstly, a rough extrapolation of the recorded incidence was performed. Approximately 25,000 inhabitants live in Lambaréné, whereby 35% of the population is below the age of 15 years [8]. The 32 children with TB enrolled in this study who resided in Lambaréné were included in the extrapolation, the results of which suggested an annual incidence of childhood TB of 366/100,000 general population in this area. This surprisingly high incidence would signify that childhood TB accounts for 23% of the total estimated TB incidence (official overall incidence estimate of 553 per 100,000 general population) [4]. This high percentage of childhood TB burden appears to be plausible but is considerably higher than that from other sub-Saharan high TB burden countries (e.g. 16.1% in Democratic Republic Congo, Uganda, South Africa) [7]. Assuming a comparable childhood TB burden of 16% for the area of Lambaréné, the overall TB incidence would be 800 per 100,000 general population and thereby exceed the official estimates by 45%. In the given context of a high HIV rate and TB-related stigma [10], under-reporting of adult TB cases appears to be more likely than over-reporting of paediatric TB cases. The assumption of an overall underestimated TB burden in Gabon is further fuelled by the inadequately low number of smears performed for TB diagnosis, i.e. only one smear per 100,000
people per year, and an inadequate laboratory capacity throughout the country for processing samples for mycobacterial culture or molecular diagnosis [4]. Additionally, a poorly maintained and functioning notification system possibly contributes to an underestimate of the true TB burden. The deficiency in reporting TB systematically is exemplified by this analysis of an incomplete paediatric TB register and further strengthened by the lack of adding the paediatric TB cases to the general TB notification register of the hospital.

Most children of this cohort were treated with the triple regimen of RHZ without ethambutol. Current WHO guidelines recommend RHZE as the treatment for all children with childhood TB who reside in areas with unknown isoniazid resistance levels or an HIV prevalence of >5 % among TB patients [11, 12]; both factors apply to Gabon. However, in Gabon, the official treatment guidelines of the NTP state that the use of ethambutol for children weighing <30 kg is contra-indicated. In the light of emerging drug resistance and the unavailability of drug sensitivity testing (DST) in Gabon, adapting the national paediatric treatment guidelines to the WHO recommendation would appear to be a sensible step.

The treatment success rate of 58 % corresponds to the treatment success rate of 55 % previously published for new smear-positive patients in Gabon in 2009 [4, 13]. No clinical suspicion of drug-resistant TB could be derived from evaluation of this child cohort; however, at least a quarter of patients were registered as lost to follow-up. While officially not a single case of MDR TB was reported in Gabon in 2010 [4], MDR and XDR TB are emerging [6], and MDR TB is estimated to be around 2.2 and 9.4 % in new and retreatment cases, respectively [4]. As DST has not been performed for several years, no official secondline therapy recommendation has been established, and drugs for treatment of MRD-TB would most likely not be readily available. Cure rates need to be raised by improving treatment adherence and follow-up and recurrent TB drug supply shortages need to be banned to reduce the present risk for drug-resistant TB.

The percentage of HIV tests performed in the paediatric TB cohort was very low considering any patient suspected or treated for TB should be tested for HIV co-infection [14]. Now, 2 years later, HIV testing is systematically performed for all TB suspected children seen at the paediatric ward of the Albert Schweitzer Hospital, in accordance to the national and international recommendations [11].

Our study was limited by its retrospective design, small sample size and the partly incomplete dataset; consequently, a detailed discussion of all of the above-mentioned results would not be appropriate. Generalization of the observations from Lambaréné to the rest of the country needs to be considered with caution.

Locally available infrastructure for TB control is very limited, and management of TB patients is integrated in the busy routine patient care which does not allow TB
control activities beyond individual patient care. Thus, components of TB control, such as isolation, infection control, directly observed therapy, or contact screening, are not applied. In the light of the important and possibly still growing TB disease burden in Gabon, there is an acute need for increased TB control measures on all levels. Despite being ranked among the top richest countries of Africa, about one-third of the Gabonese population lives in poverty as the income distribution is skewed and social indicators show poor values [5]. Within the international framework of worldwide TB control efforts, criteria other than the national per capita income may be more adequate as an indicator for international funds allocation and thereby more effective for joint efforts to reduce the global TB burden in all affected populations.

CONCLUSIONS

This retrospective snapshot on childhood TB in Lambaréné indicates that the paediatric and general TB burden is underestimated in Gabon and identifies deficiencies within all main pillars of the DOTS Strategy. The country urgently needs to strengthen TB control. However, if TB control is not prioritized on a national level through increasing awareness and the necessary infrastructure is not established through the allotment of financial and human resources, international organizations should shoulder some responsibility and not ignore the ongoing TB burden in poor populations of countries considered too rich for international support.

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CONFLICT OF INTEREST

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