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Tuberculosis case burden and treatment outcomes in children, adults and older adults, Vanuatu, 2007–2011

M. Tagaro,[1] A. D. Harries,[2,3] B. Kool,[4] S. Ram,[5] K. Viney,[6] B. Marais,[7] L. Tarivonda[8]

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Setting: All five DOTS centres in Vanuatu.
Objectives: To determine across the age spectrum the tuberculosis (TB) case burden, disease pattern and treatment outcomes in patients registered between 2007 and 2011.
Design: Retrospective cohort study involving reviews of TB registers and treatment cards.
Results: Of 588 TB patients, 142 (24%) were children (aged 0–14 years), 327 (56%) adults (aged 15–54 years) and 119 (20%) were older adults (aged ⩾55 years; subdivided into 55–64 and ⩾65 years); 568 were new patients, 13 had been treated previously and 7 had unknown status. Compared with adults, children with new TB had a higher prevalence of extra-pulmonary TB (75% vs. 34%, OR 5.7, 95%CI 3.6–9.0) and a lower prevalence of smear-positive pulmonary TB (11% vs. 45%, OR 0.15, 95%CI 0.1–0.3), while older adults with new TB had a higher prevalence of smear-negative pulmonary TB (38% vs. 21%, OR 2.4, 95%CI 1.5–3.8). Overall TB treatment success was 83%, but in the second category of older adults (⩾65 years) treatment success was 67% and case fatality was 18%.
Conclusion: Children and older adults constitute 45% of the TB burden in Vanuatu. Differences in disease patterns and poorer treatment outcomes in older adults have implications for policy and practice.

Vanuatu is an island country located in the South Pacific. The National Tuberculosis Programme (NTP) was started in Vanuatu in the early 1980s, and the DOTS strategy[1] was introduced in 1999. Each year, around 110–130 patients with tuberculosis (TB) are diagnosed and registered for treatment, of whom 30–50 have new smear-positive pulmonary TB (PTB).[2] The NTP initially only reported on outcomes of smear-positive PTB patients, but in the last 5 years this has been extended to all patients with TB (i.e., including those with smear-negative PTB and extra-pulmonary TB [EPTB]).

The NTP is interested in establishing the case burden, pattern of disease and treatment outcomes of all patients registered with TB in the last 5 years in Vanuatu, and in particular among children and older adults, for whom no data from the country have been published. Ascertaining the TB burden in children is important, as children are a vulnerable group, and childhood TB reflects ongoing TB transmission from adults in the community and is an indicator of the effectiveness of TB prevention and infection control measures in the population.[3] TB may present and manifest itself differently in older compared with younger adults.[4] Furthermore, older adults are at high risk of non-communicable diseases, especially diabetes mellitus. It is well established that the risk of TB among people with diabetes increases by two- to three-fold,[5] with those who later develop TB having poorer treatment outcomes.[6]

Although information about the burden and pattern of disease and treatment outcomes in different age groups is available in TB patient registers and treatment cards, the data have not been formally analysed or interpreted at the country level. This is important to determine whether different strategies might be needed for diagnosis and treatment in patients in different age groups.

The aim of the present study was to determine the TB case burden, the pattern of disease and treatment outcomes in child, adult and older adult patients registered in Vanuatu between 2007 and 2011.

METHODS

Study design

This was a retrospective cohort study involving a review of records.

Setting

General setting

Vanuatu is made up of 83 islands divided into six provinces, with an estimated general population of 234 032.[7] The average life expectancy in Vanuatu is 63 years for males and 66 years for females. Vanuatu is classified as a lower middle-income country according to the World Bank, with an annual gross national income of US$1006–3975 per capita.[8] In each province, there is a provincial hospital staffed by doctors and nurses; peripheral health care in the country is provided by 32 health centres, 99 dispensaries and 222 aid posts. Health care in the government sector and in the provincial hospitals is free of charge.

National TB control

Vanuatu has a central NTP unit consisting of a programme manager, a deputy manager and a monitoring and evaluation officer situated in the Ministry of Health in Port Vila, the capital city. Five DOTS centres in provincial hospitals situated in the provinces of Shefa, Tafea, Malampa, Sanma and Penama offer smear microscopy services and are staffed by a provincial TB officer and a TB nurse.

TB management

Individuals with presumptive TB are identified using passive case finding based on cough of >2 weeks' du-

AFFILIATIONS
1 National TB Control Programme, Port Vila, Vanuatu
2 International Union Against Tuberculosis and Lung Disease, Paris, France
3 London School of Hygiene & Tropical Medicine, London, UK
4 School of Population Health, The University of Auckland, Auckland, New Zealand
5 College of Medicine, Nursing and Health Sciences, Fiji National University, Suva, Fiji
6 Secretariat of the Pacific Community, Nouméa, New Caledonia
7 The Sydney Emerging Infections and Biosecurity Institute, The University of Sydney, Sydney, New South Wales, Australia
8 Department of Public Health, Ministry of Health, Port Vila, Vanuatu

CORRESPONDENCE
Markleen Tagaro
National TB Programme
PMB 9009
Port Vila
Vanuatu
Tel: (+678) 22512
Fax: (+678) 25438
e-mail: mtagaro@vanuatu.gov.vu

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ration,[9] and are asked to submit three sputum specimens for smear examination under light microscopy at one of the DOTS centres. Patients with acid-fast bacilli (AFB) in at least one sputum specimen are diagnosed with smear-positive PTB. AFB smear-negative patients are referred for chest X-ray (CXR) and clinical assessment, and based on the findings a diagnosis of smear-negative PTB may be made. Patients with EPTB are diagnosed per national guidelines.[9]

All patients diagnosed with TB (children and adults) are registered and treated with the standardised regimen. For new patients this consists of a 2-month intensive phase of daily rifampicin, isoniazid, pyrazinamide and ethambutol (2RHZE) under direct observation in hospital, followed by a 4-month continuation phase with daily rifampicin and isoniazid (4RH) taken at home. In the continuation phase, treatment is directly observed by a community nurse or a treatment partner.[9] Retreatment patients are treated with a standardised regimen.[9] All patients are followed up in a standardised manner during treatment, with final treatment outcomes defined as cured, treatment completed, died, lost to follow-up (recorded in Vanuatu registers as defaulted), transferred out and failed.[9] Case finding details and treatment outcomes are recorded in the TB treatment cards and TB patient registers maintained in each DOTS centre.

Study participants

The study included all TB patients registered over a 5-year period between 2007 and 2011. Participants were stratified into three main groups: children (in two age groups of 0–4 and 5–14 years), adults aged 15–54 years and older adults aged ⩾55 years, subdivided into 55–64 and ⩾65 years.

Data variables, analysis and statistics

Data variables related to the study objectives were collected from the TB registers and treatment cards of each of the DOTS centres during the first 6 months of 2013. These data were transcribed onto a paper-based collection form and then single-entered using EpiData Version 3.1 (EpiData Association, Odense, Denmark). Case finding and treatment outcomes were analysed in relation to the different age groups as defined above, and these were compared using the χ^2 test, with odds ratios (ORs) used to compare case finding details and relative risks (RRs) used to compare treatment outcomes. Patterns of TB and treatment success rates were also compared between males and females; 95% confidence intervals (CIs) were used and levels of significance were set at 5%.

Ethics

Ethical approval was obtained from the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. Permission for the study was obtained from the Director of Public Health, Ministry of Health, Port Vila, Vanuatu.

RESULTS

During the 5-year period, of the 588 registered TB patients, 330 (56%) were male and 257 (44%) female (in one patient sex was not recorded); 142 (24%) were children aged 0–14 years, 327 (56%) were adults aged 15–54 years and 119 (20%) were older adults aged ⩾55 years. The total annual TB burden and the annual burden stratified by age group remained stable during the study period (Figure).

Of the 588 TB patients, 568 (97%) were new cases, 13 (2%) had been previously treated for TB and 7 (1%) had no record of TB type or category. Of the 568 new patients, 58% had PTB and 42% had EPTB. There were significant differences in the patterns of disease observed in the different age groups (Table 1). Using adults aged 15–54 years as reference, there was a significantly higher prevalence of EPTB (75% vs. 34%, OR 5.7, 95%CI 3.6–9.0), a significantly lower prevalence of smear-positive PTB (11% vs. 45%, OR 0.15, 95%CI 0.1–0.3) and a similar prevalence of smear-negative PTB (14% vs. 21%, OR 0.62, 95%CI 0.4–1.1) among new TB cases in children aged 0–14 years; these differences were more pronounced in younger children aged 0–4 years. Compared with adults aged 15–54 years, there was a significantly higher prevalence of smear-negative PTB (38% vs. 21%, OR 2.4, 95%CI 1.5–3.8) and a similar prevalence of smear-positive PTB (37% vs. 45%, OR 0.7, 95%CI 0.4–1.1) and EPTB (25% vs. 34%, OR 0.6, 95%CI 0.4 – 1.03) in older adults aged ⩾55 years. In new patients,

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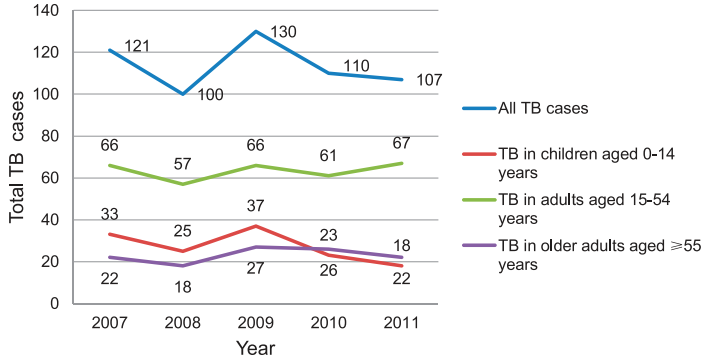

FIGURE Annual burden of TB, stratified by children, adults and older adults, Vanuatu, 2007–2011. TB = tuberculosis.

TABLE 1 Type and category of TB reported in Vanuatu, 2007–2011, stratified by age group

Age category, years	Registered patients *n*	New			Previously treated			Not recorded *n* (%)*
		Smear-positive PTB *n* (%)*	Smear-negative PTB *n* (%)*	EPTB *n* (%)*	Relapse *n* (%)*	Failure *n* (%)*	Treatment after LTFU *n* (%)*	
Children 0–4	65	1 (1)	3 (5)	57 (88)	0	0	0	4 (6)
Children 5–14	77	14 (18)	16 (21)	45 (58)	1 (1.5)	0	0	1 (1.5)
Adults 15–54	327	143 (44)	65 (20)	109 (33)	3 (1)	1 (<1)	5 (2)	1 (<1)
Adults 55–64	72	26 (36)	29 (40)	15 (21)	0	1 (1.5)	1 (1.5)	0
Adults ⩾65	47	16 (34)	15 (32)	14 (30)	1 (2)	0	0	1 (2)
All patients	588	200 (34)	128 (22)	240 (41)	5 (1)	2 (<1)	6 (1)	7 (1)

*Row percentages.
TB = tuberculosis; PTB = pulmonary TB; EPTB = extra-pulmonary TB; LTFU = loss to follow-up.

the patterns of TB were not significantly different between males and females (smear-positive PTB, males 32%, females 39%; smear-negative PTB, males 23%, females 22%; EPTB, males 45%, females 39%).

Of the 240 patients with EPTB, the specific site of disease was recorded in only 135 (56%). In those patients in whom site of disease was recorded, the four most common sites were peripheral TB lymph node disease (*n* = 53, 72% in children), TB pleural effusion (*n* = 36, 83% in adults ⩾15 years), TB of the spine (*n* = 33, 96% in adults ⩾15 years) and TB meningitis (*n* = 11, 55% in children).

TB treatment outcomes among all new TB patients by age group are shown in Table 2. Taking adults aged 15–54 years as reference, the only significant differences in treatment outcomes between the groups were in older adults aged ⩾65 years, in whom the treatment success rate was lower (67% vs. 83%, RR 0.8, 95%CI 0.6–0.98) and death during treatment (case fatality) was higher (18% vs. 6%, RR 2.8, 95%CI 1.3–6.0). Overall treatment success rates were not significantly different between males and females (81% vs. 86%).

DISCUSSION

This is the first study to investigate variations in the burden and pattern of TB and treatment outcomes by age in Vanuatu. Children constituted about one quarter and older adults about one fifth of the total TB burden during the 5-year period reviewed (2007–2011). In all age groups, the majority of the patients were new TB cases, with children having a significantly higher prevalence of EPTB and older adults having a significantly higher prevalence of smear-negative PTB than adults aged 15–54 years. Where it was recorded, the most common site of EPTB in children was peripheral lymph node disease.

These findings in children are very similar to those recently reported in India and Bhutan, where over two thirds of children with TB had extra-pulmonary disease, with TB lymph node disease being the most common site.[10,11] They differ, however, from patterns of disease reported from Africa,[12,13] and from those expected from the natural history of the disease,[14] where pulmonary disease is most common, particularly smear-negative PTB. This may be influenced by the effects of human immunodeficiency virus (HIV) co-infection in Africa,[12,13] but may also reflect limited access to CXR in the study setting. Our findings in older adults are also similar to those reported recently in India,[15] although the prevalence of smear-positive PTB was higher among older adult patients in India. In a country with limited diagnostic resources such as Vanuatu, it is possible that older patients have a higher prevalence of chronic lung disease with various aetiologies that are potentially misdiagnosed as smear-negative PTB based on negative sputum smears and abnormal CXR.

The treatment success rate for all new TB patients in this study was 83%, approaching the World Health Organization target of 85%.[16] Outcomes in children were excellent, particularly among those aged 5–14 years, consistent with results reported from India and Bhutan.[10,11] This is in contrast to TB treatment outcomes that may be worse in children than in adults in low-income countries in sub-Saharan Africa, largely due to the additional morbidity and mortality resulting from co-infection with HIV.[12,13] The poor outcomes among adults aged ⩾65 years in the present study are in line with the recent report from India showing poor treatment outcomes among older TB patients, particularly among those aged ⩾70 years.[15] The high death rates among older adults observed in our study could be due in part to comorbidities such as diabetes mellitus, hypertension and associated cardiovascular diseases,

TABLE 2 TB treatment outcomes in new TB patients stratified by children, adults and older adults in Vanuatu, 2007–2011

Age category years	Enrolled into treatment *n*	Treatment success* *n* (%)†	Loss to follow-up *n* (%)†	Failed *n* (%)†	Died *n* (%)†	Transfer out *n* (%)†	Not recorded *n* (%)†
Children 0–4	61	48 (79)	2 (3)	0	4 (7)	3 (5)	4 (6)
Children 5–14	75	69 (92)	3 (5)	0	1 (1)	1 (1)	1 (1)
Adults 15–54	317	266 (84)	10 (3)	3 (1)	20 (6)	12 (4)	6 (2)
Adults 55–64	70	56 (80)	1 (1.5)	1 (1.5)	9 (13)	3 (4)	0
Adults ⩾65	45	30 (67)	0	1 (2)	8 (18)	3 (7)	3 (6)
All patients	568	469 (83)	16 (3)	5 (1)	42 (7)	22 (4)	14 (2)

*Includes cured and treatment completed.
†Row percentages.
TB = tuberculosis.

which are becoming increasingly prevalent in Vanuatu.[17] Diabetes in TB patients in particular is known to be associated with an increased risk of death during anti-tuberculosis treatment.[6]

The strengths of this study are the population-based national sample of patients, collected over a 5-year period with over 500 patients registered in the database. The results are therefore likely to be representative of the TB population residing in Vanuatu. The study was conducted and reported according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[18] However, the study findings need to be interpreted in the light of several limitations. Due to a lack of human resources, data were single-entered and there may have been some unidentified errors in this transcription. The use of secondary data from TB registers and treatment cards resulted in some missing data. In particular, the site of EPTB was often missing, vague or recorded as 'other'. In the majority of the cases, we were unable to verify how the diagnosis of EPTB was made, although in Vanuatu this is usually based on circumstantial evidence rather than on histology or microbiology.

Despite these limitations, the findings from this study have implications for policy and practice. Given that a quarter of TB cases each year occur in children, there is a need to engage more actively in contact tracing and isoniazid preventive therapy (IPT) to reduce the burden of disease among this vulnerable population. Although national guidelines recommend the use of IPT in child contacts (aged <5 years) of index smear-positive PTB cases, we do not know if these are followed, and this should be an area for further operational research. The high rates of childhood TB highlight the need to support the recently introduced 2011 National TB Treatment Guidelines, which place more emphasis on the diagnosis and management of TB in children.[9] More attention needs to be paid to the criteria for diagnosing PTB and EPTB in children, and further operational research is needed to understand how the diagnosis of EPTB is made in the country, and whether this differs from province to province.

The poorer outcomes identified among older adults reinforces the need for clinical research to better understand the profile of disease among this age group represented under the diagnosis of 'smear-negative PTB', as has been done in other countries.[19] The recent introduction of routine screening of TB patients for diabetes, the diagnosis of which impacts TB outcomes but is amenable to treatment, has the potential to reduce the TB burden and improve TB treatment outcomes among older adults in Vanuatu.[6,20]

In conclusion, this observational study has shown that childhood TB and TB in older adults together constitute nearly one half of all TB cases in Vanuatu, with important differences in the pattern of disease in the different age groups. Older adult patients had a lower rate of treatment success and higher mortality; more attention needs to be paid to improving treatment outcomes in this group of patients.

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Contexte : Les cinq centres DOTS du Vanuatu.
Objectifs : Déterminer le fardeau de la tuberculose (TB) à travers les classes d'âge, le profil de la maladie et les résultats du traitement des patients enregistré entre 2007 et 2011.
Schema : Etude de cohorte rétrospective impliquant des registres de TB et des cartes de traitement.
Resultats : Sur 588 patients enregistrés, 142 (24%) étaient des enfants (âgés de 0–14 ans), 327 étaient des adultes (âgés de 15–54 ans) et 119 des adultes plus âgés (âgés de ⩾55 ans, subdivisés en 55–64 et ⩾65 ans). Parmi eux, 568 étaient des nouveaux patients, et 13 avaient déjà été traités ; pour 7 d'entre eux, le statut était inconnu. Comparés aux adultes, les enfants avec une TB nouvelle avaient une plus grande prévalence de TB extra pulmonaire (75% contre 34% ; OR 5,7 ; IC95% 3,6–9,0) et une prévalence plus faible de TB pulmonaire frottis positif (11% contre 45% ; OR 0,15 ; IC95% 0,3–0,3). Les adultes âgés de ⩾55 ans avaient une prévalence plus élevée de TB pulmonaire à frottis négatif (38% contre 21% ; OR 2,4 ; IC95% 1,5–3,8). Le succès du traitement de la TB a été de 83% pour l'ensemble du groupe, mais seulement de 67% pour les patients âgés de ⩾65 ans avec un taux de létalité de 18%.
Conclusion : Les enfants et les adultes plus âgés constituent 45% du fardeau de la TB au Vanuatu. Les différences constatées en termes de profil de la maladie et de résultats thérapeutiques moins bons chez les adultes âgés ont des implications en matière de politique et de pratiques.

Marco de referencia: Los cinco centros de administración del DOTS en Vanuatu.
Objetivos: Determinar la carga de morbilidad por tuberculosis (TB) en las diferentes edades, las características de la enfermedad y los desenlaces terapéuticos de los pacientes registrados entre el 2007 y el 2011.
Método: Se llevó a cabo un estudio retrospectivo de cohortes con examen de los registros de TB y las tarjetas de tratamiento.
Resultados: Se registraron 588 pacientes con TB, de los cuales 142 (24%) niños (de 0 a 14 años de edad), 327 (56%) adultos (de 15 a 54 años de edad) y 119 (20%) adultos (⩾55 años, divididos en 55–64 y ⩾65 años). Hubo 568 casos nuevos, 13 con antecedente de tratamiento antituberculoso y 7 cuya situación se desconocía. En comparación con los adultos, los casos nuevos de TB en los niños exhibieron una mayor prevalencia de localización extrapulmonar (75% contra 34%; OR 5,7; IC95% de 3,6 a 9,0) y una prevalencia más baja de TB con baciloscopia positiva (11% contra 45%; OR 0,15; IC95% de 0,1 a 0,3); los casos nuevos en los adultos mayores (de ⩾55 años) presentaron una prevalencia más alta de TB pulmonar con baciloscopia negativa (38% contra 21%; OR 2,4; IC95% de 1,5 a 3,8). En general, la tasa de tratamiento exitoso fue 83%, pero en los ancianos (⩾ 65 años) se alcanzó un tratamiento eficaz en el 67% y se observó un índice de letalidad de 18%.
Conclusión: Los niños y los adultos mayores representan el 45% de la carga de morbilidad por TB en Vanuatu. Las diferencias en las características de la enfermedad y los desenlaces terapéuticos más desfavorables en los adultos mayores tienen consecuencias en las políticas y en la práctica clínica.

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