



PNG SUPPLEMENT

Gaps in tuberculosis care in West Sepik Province of Papua New Guinea

T. Kelebi,¹ K. C. Takarinda,^{2,3} R. Commons,^{4,5} B. Sissai,¹ J. Yowei,¹ M. Gale⁴<http://dx.doi.org/10.5588/pha.18.0057>**Setting:** Papua New Guinea (PNG), a low-resource country with a high tuberculosis (TB) burden.**Objective:** To describe the characteristics, treatment outcomes and risk factors for unfavourable outcomes among patients registered for first-line tuberculosis (TB) treatment between 1 January 2014 and 31 December 2016 in West Sepik Province.**Design:** This was a retrospective cohort study of routinely collected programme data.**Results:** Of 1058 cases, 50.7% were male and 38.8% were aged <15 years; 43.1% were extrapulmonary TB cases and 280 (26.5%) were bacteriologically confirmed. No human immunodeficiency virus (HIV) status was recorded for 74.7% of cases. Of 1019 (96.3%) patients with a recorded outcome, 779 (76.4%) were favourable and 240 (23.6%) were unfavourable. On multivariable logistic regression, increasing age was associated with an increased odds of an unfavourable outcome (adjusted OR [aOR] 1.06 per every 5-year increase, 95%CI 1.02–1.11; $P = 0.006$) and being a retreatment case was associated with a reduced odds of an unfavourable outcome compared to new cases (aOR 0.54, 95%CI 0.31–0.93; $P = 0.027$).**Conclusion:** This study identified substantial gaps in TB care, including low rates of bacteriological diagnosis and HIV testing, and high rates of loss to follow-up, highlighting the need to strengthen TB control efforts, including support for new cases.

Tuberculosis (TB) is a major global public health disease, with an estimated 10.4 million new cases and 1.7 million deaths occurring in 2016. Of these, the majority of new cases and deaths occurred in low- and middle-income countries (LMICs).¹ Completing TB treatment remains a challenge due to multiple issues in LMIC countries, including socio-economic factors, access to health facilities and trained staff, long treatment regimens and poor health literacy.^{2–5}

The Western Pacific Region accounted for 17% of the estimated incident TB cases in 2016. The reported successful TB treatment outcomes in 2015 for the Western Pacific Region were the highest among all WHO Regions, at 92%.¹ While this is encouraging for TB control, it was not the case for Papua New Guinea (PNG), which is one of 14 priority countries worldwide with a triple burden of TB, multidrug-resistant TB and TB-human immunodeficiency virus (HIV) co-infection. In 2016, PNG had the highest estimated

annual TB incidence rate in the Western Pacific Region, at 432 cases per 100 000 population.¹ A recently published analysis of TB in PNG for the period 2008–2016 reported a treatment success rate of 64% and a loss to follow-up (LTFU) rate of 19%.⁶

While TB programmes in different international settings have examined the risk factors for poor TB outcomes in their context, there is limited understanding of the factors that drive poor treatment outcomes at a national or provincial level in PNG.^{2–4,7,8} The present study aimed to determine TB treatment outcomes and the risk factors for poor outcomes of patients treated for drug-susceptible TB in West Sepik Province, PNG.

STUDY POPULATION, DESIGN AND METHODS

Design

This was a retrospective cohort study of routinely collected TB programme data.

General setting

Situated in the South Pacific Ocean north of Australia, PNG has a population of more than 7 million people. PNG is ethnically and linguistically diverse, with >80% of the population residing in rural areas.⁹ Despite recent expansion of the National TB Programme, substantial challenges remain in TB diagnosis and treatment, drug management, and recording and reporting systems.⁶

Local setting

West Sepik Province is situated at the north-western tip of mainland PNG and shares a border with Indonesia. It is one of the least developed provinces of PNG, with a population of approximately 248 000.^{10–12} There is one provincial hospital, two district hospitals, 36 health centres and 139 aid posts.

Limited tools for TB diagnosis are available at two facilities: Raihu District Hospital in Aitape-Lumi District and Sandaun Provincial Hospital in Vanimo, the provincial capital. Ziehl-Neelsen microscopy is conducted at these sites on sputum and other specimens such as lymph node biopsies. X-ray is also available in the two facilities. Xpert[®] MTB/RIF testing (Cepheid, Sunnyvale, CA, USA) is performed only in Sandaun Provincial Hospital for patients with presumptive drug-resistant TB (DR-TB). Specimens that are rifampicin-resistant on Xpert are sent to the Central Public Health Laboratory (Port Moresby, PNG) for culture before being sent to the Supranational Reference Laboratory (Brisbane, QLD, Australia) for drug susceptibility testing.

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KEY WORDS

rural health; loss to follow-up; HIV

Received 12 August 2018
Accepted 11 October 2018

PHA 2019; 9(S1): S68–S72
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TABLE 1 Demographic and clinical characteristics of all first-line TB patients registered in Sandaun Provincial Hospital and Raihu District Hospital, West Sepik Province, Papua New Guinea, 1 January 2014–31 December 2016

Variables	Sandaun Provincial Hospital <i>n</i> (%)	Raihu District Hospital <i>n</i> (%)	Total <i>n</i> (%)
Total	769	289	1058
Sex			
Male	378 (49.2)	158 (54.7)	536 (50.7)
Female	391 (50.8)	131 (45.3)	522 (49.3)
Age, years, median [IQR]	21 [6–32]	23 [7–45]	21 [7–35]
0–4	151 (19.6)	49 (17.0)	200 (18.9)
5–14	149 (19.4)	62 (21.5)	211 (19.9)
15–24	152 (19.8)	43 (14.9)	195 (18.4)
25–44	225 (29.3)	54 (18.7)	279 (26.4)
≥45	92 (12.0)	81 (28.0)	173 (16.4)
Time to reach BMU site, h			
<3	593 (77.1)	228 (78.9)	821 (77.6)
≥3	167 (21.7)	58 (20.1)	225 (21.3)
Not recorded	9 (1.2)	3 (1.0)	12 (1.1)
HIV status			
Positive	13 (1.7)	1 (0.3)	14 (1.3)
Negative	187 (24.3)	67 (23.2)	254 (24.0)
Not recorded	569 (74.0)	221 (76.5)	790 (74.7)
Type of TB			
New	686 (89.2)	260 (90.0)	946 (89.4)
Retreatment	83 (10.8)	29 (10.0)	112 (10.6)
Site of TB			
Pulmonary	418 (54.4)	184 (63.7)	602 (56.9)
Extrapulmonary	351 (45.6)	105 (36.3)	456 (43.1)
Classification of TB			
Bacteriologically confirmed	221 (28.7)	59 (20.4)	280 (26.5)
Clinically diagnosed	548 (71.3)	230 (79.6)	778 (73.5)

TB = tuberculosis; IQR = interquartile range; BMU = Basic Management Unit; HIV = human immunodeficiency virus.

Study participants

All patients receiving first-line TB treatment in West Sepik Province registered between 1 January 2014 and 31 December 2016 were recruited. Patients diagnosed with DR-TB were excluded.

Data sources

The data for this study were collected from TB registers at Sandaun Provincial Hospital and Raihu District Hospital. The variables collected were site, registration number, sex, age, address, site of TB, HIV status, treatment history, result of bacteriological confirmation and treatment outcome. The TB Basic Management Unit (BMU) registration number, a unique identifier, was also collected to enable data validation using double data entry in EpiData v.3.1 (EpiData Association, Odense, Denmark).

Case and outcome definitions were based on the PNG National TB Management Protocols in accordance with World Health Organization guidance.^{12,13} Patient residence was categorised according to the time required to travel from home to the BMU site as <3 h and >3 h. Travel time was determined by surveying 50 local residents from each BMU site.

Analysis and statistics

Statistical analysis was performed using EpiData v.3.1 and Stata v.15 (StataCorp, College Station, TX, USA).

Categorical variables were reported as numbers (percentages) and continuous variables as medians (interquartile range [IQR]). An unfavourable treatment outcome was defined as treatment failure, death or LTFU, and a favourable treatment outcome was defined as cured or treatment completed. Patients with an outcome of 'not evaluated' were excluded, as the majority were known to have transferred out. Risk factors for poor outcomes were assessed using logistic regression to determine unadjusted and multivariable-adjusted odds ratios (aORs) with their 95% confidence intervals (95%CI). $P < 0.05$ was considered significant.

Ethical approval

Ethics approval was obtained from the PNG Medical Research Advisory Committee (Port Moresby, PNG) and the Alfred Hospital Ethics Committee (Melbourne, VIC, Australia).

RESULTS

Of the 1058 cases registered on first-line TB treatment during the study period, the median age was 21 years [IQR 7–35]; 411 (38.8%) of all cases were aged <15 years. Males made up 50.7% of the total cohort (Table 1).

The majority of the cases were from Sandaun Provincial Hospital (72.7%). Time from residence to the BMU site was similar for cases from both hospitals.

ACKNOWLEDGEMENTS

This research was conducted as part of the first Operational Research Course for Tuberculosis in Papua New Guinea (PNG). The specific training programme that resulted in this publication was developed and implemented by the Burnet Institute (Melbourne, VIC, Australia) in collaboration with the PNG Institute of Medical Research (Goroka) and University of PNG (Port Moresby), and supported by the PNG National Department of Health Emergency Response Taskforce for MDR- and XDR-TB, the National TB Programme and Western Provincial Health Office, Daru, PNG. The model is based on the Structured Operational Research and Training Initiative (SORT IT), a global partnership led by the Special Programme for Research and Training in Tropical Diseases at the World Health Organization (WHO/TDR). The authors thank the Sandaun Provincial Administration (PNG) and the West Sepik Provincial Health Authority (PNG) for their support; and H Norm, C Tilau, A Yalim, B Watoka, S Kilik, C Seim, B Afara and all the study participants. The training programme was supported by the Australian Government, as part of the Tropical Disease Research Regional Collaboration Initiative (TDRRCI), strengthening regional research collaboration in the prevention and containment of multidrug-resistant tuberculosis and malaria, a regional consortium led by the Menzies School of Health Research (Darwin, NT, Australia) and the Burnet Institute (Grant 1132089). The views expressed in this publication are the authors' alone and are not necessarily the views of the Australian or PNG Governments. The funder had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript. Conflicts of interest: none declared.

TABLE 2 Factors associated with unfavourable treatment outcomes among first-line TB patients* registered in Sandaun Provincial Hospital and Raihu District Hospital, West Sepik Province, PNG, 1 January 2014–31 December 2016

Variables	Favourable TB outcome <i>n</i> (%)	Unfavourable TB outcome <i>n</i> (%)	OR (95%CI)	aOR (95%CI)
Total	779	240		
BMU site				
Raihu District Hospital	224 (79.7)	57 (20.3)	Reference	
Sandaun Provincial Hospital	555 (75.2)	183 (24.8)	1.30 (0.93–1.81)	1.41 (1.00–2.01)
Sex				
Female	374 (75.1)	124 (24.9)	Reference	
Male	405 (77.7)	116 (22.3)	0.86 (0.65–1.15)	0.86 (0.64–1.15)
Age, 5-year increments	–	–	1.04 (1.00–1.08)	1.06 (1.02–1.11)
Time to BMU site, h				
<3	609 (76.8)	184 (23.2)	Reference	
≥3	161 (75.2)	53 (24.8)	1.09 (0.77–1.55)	1.05 (0.74–1.51)
Not recorded	9 (75.0)	3 (25.0)	1.10 (0.30–4.12)	1.18 (0.31–4.48)
HIV status				
Negative	196 (79.4)	51 (20.6)	Reference	
Positive	8 (57.1)	6 (42.9)	2.88 (0.96–8.68)	2.72 (0.88–8.39)
Not recorded	575 (75.9)	183 (24.1)	1.22 (0.86–1.74)	1.37 (0.92–2.05)
Type of TB patient				
New	686 (75.5)	223 (24.5)	Reference	
Retreatment	93 (84.5)	17 (15.5)	0.56 (0.33–0.96) [†]	0.54 (0.31–0.93) [†]
Site of TB				
Pulmonary	445 (76.3)	138 (23.7)	Reference	
Extrapulmonary	334 (76.6)	102 (23.4)	0.98 (0.73–1.32)	0.81 (0.57–1.15)
Classification of TB				
Bacteriologically confirmed	213 (78.3)	59 (21.7)	Reference	
Clinically diagnosed	566 (75.8)	181 (24.2)	1.15 (0.83–1.61)	1.30 (0.84–1.97)

*Excluding 39 patients who did not have an outcome evaluated.

[†] $P < 0.05$.

TB = tuberculosis; OR = odds ratio; CI = confidence interval; aOR = adjusted OR; BMU = Basic Management Unit; HIV = human immunodeficiency virus.

Data on HIV status was recorded for only 268 (25.3%) patients, 14 (5.2%) of whom were HIV-positive. Extrapulmonary TB (EPTB) accounted for 456 (43.1%) of all TB cases; 280 (26.5%) of all cases were bacteriologically confirmed. Of 99 patients tested using Xpert, 11 were positive.

After excluding 39 patients who were not evaluated, 779/1019 (76.4%) patients had a favourable treatment outcome, while 177 (17.3%) were lost to follow-up, 47 (4.6%) died and 16 (1.6%) had treatment failure (Table 2).

In multivariable logistic regression, increasing age was associated with an increased odds of an unfavourable outcome (aOR 1.06 per each 5-year increase, 95%CI 1.02–1.11, $P = 0.006$); retreatment cases were associated with a reduced odds of an unfavourable outcome compared to new cases (aOR 0.54, 95%CI 0.31–0.93, $P = 0.027$). As the majority of patients with an unfavourable outcome were lost to follow-up, this group was explored separately. Only registration at Sandaun Provincial Hospital was associated with an increased odds of LFTU (aOR 1.88, 95%CI 1.23–2.86, $P = 0.003$).

DISCUSSION

This study, conducted in rural PNG, identified high rates of unfavourable treatment outcomes among notified TB patients during a 3-year period. Cohort characteristics were similar to other TB cohorts described recently in PNG, with high rates of EPTB, a high proportion of child patients and low rates of bacteriological and HIV testing.⁶

In contrast to what has been described at the national⁶ and global¹ levels, this study found that retreatment cases had a reduced risk of unfavourable outcomes compared to new cases. As the main contributing factor to unfavourable outcome was LFTU, it is possible that staff and patients had a greater commitment to treatment completion when retreated.

A key strength of this study is that it captured all the TB cases registered in West Sepik Province during the study period. The results will be important in guiding efforts to close the gap between TB policy and practice in West Sepik Province and throughout PNG.

One limitation of our study is its reliance upon previously collected programme data that we could not validate. Although an approximate measure of time to BMU was used to evaluate the patients' proximity to care, this may not have captured other elements that could affect access. Furthermore, the cut-offs used for time to BMU, while based on local perception of accessibility, may have been too broad to identify small differences.

The study aimed to determine the risk factors for unfavourable outcomes, however, the results may be impacted by the substantial proportion of patients for whom data variables were not recorded, including HIV status. Despite PNG guidelines that require universal HIV testing for patients diagnosed with TB, this practice is not consistently followed across the country,⁶ highlighting a significant gap between current practice and national targets.¹⁴ The factors that contribute to the low rate of testing probably include a lack of appropriate pre-test counselling and regular stock-outs of consumables.

The study highlights the need to improve TB diagnostic pathways in West Sepik Province. Implementation of Xpert as a first-line diagnostic test for all presumptive TB cases will play an important role in increasing the proportion of bacteriologically confirmed cases and in appropriately diagnosing EPTB, child TB and DR-TB.^{15,16} Although this recommendation has been included in the most recent national guidelines, a lack of material and human resources have prevented it from being implemented.

While not a focus of this study, the emergence of DR-TB in PNG is a matter of concern. During the study period, 11 cases of DR-TB were diagnosed in West Sepik. It is likely that our study cohort of patients on first-line treatment included patients with undiagnosed DR-TB. Effective implementation of Xpert is a key element in the response to DR-TB.

It is unclear whether the high number of EPTB cases diagnosed in this study represent the true disease burden or is due to overdiagnosis. The site of EPTB disease was not reliably captured in TB registers and therefore could not be described in this study. Improving the diagnostic accuracy of EPTB, through both clinical and laboratory methods, is important to avoid unnecessary TB treatment and to ensure that patients receive appropriate care for diagnoses other than TB.

Given that LTFU was the major contributor to unfavourable treatment outcomes, there is a need to examine the reasons for LTFU. Qualitative research with TB patients and staff could provide insight into the causes of LTFU.

In conclusion, this study highlights the value of using routinely collected data to identify gaps in TB control in West Sepik Province. The findings demonstrate the need to improve TB diagnosis, including bacteriological confirmation and clinical diagnosis of EPTB, improve HIV testing rates and address the factors contributing to LTFU.

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Contexte : La Papouasie Nouvelle Guinée (PNG) est un pays à faibles ressources durement frappé par la tuberculose (TB).

Objectif : Décrire les caractéristiques, les résultats du traitement et les facteurs de risque de résultats défavorables parmi les patients enregistrés en vue d'un traitement de TB de première ligne entre le 1^e janvier 2014 et le 31 décembre 2016 dans la province de West Sepik.

Schema : Une étude rétrospective de cohorte de données de programme recueillies en routine.

Resultats : Sur 1058 cas, 50,7% ont été des hommes, 38,8% avaient <15 ans. Il y a eu 43,1% de cas de TB extra pulmonaire et 280 des 1058 cas (26,5%) ont été confirmés par bactériologie. Le statut de l'infection par le virus de l'immunodéficience humaine (VIH) n'a pas

été enregistré pour 74,7% des cas. Sur 1019 (96%) patients dont l'évolution est connue, 779 (76,4%) ont eu un résultat favorable et 240 (23,6%), un résultat défavorable. En régression logistique multivariées, l'âge croissant a été associé à un risque croissant de résultat défavorable (OR ajusté [ORa] 1,06 par tranche de 5 années d'âge ; IC 95% 1,02–1,11 ; $P = 0,006$) et le fait d'être en retraitement a été associé à un risque réduit de résultats défavorable comparé à celui des nouveaux cas (ORa 0,54 ; IC 95% 0,31–0,93 ; $P = 0,027$).

Conclusion : Cette étude a identifié des lacunes majeures dans la prise en charge de la TB, notamment des taux faibles de diagnostic bactériologique et de recherche du VIH ainsi que des taux élevés de pertes de vue. Ceci met en lumière le besoin de renforcer les efforts de lutte contre la TB notamment le soutien aux nouveaux cas.

Marco de Referencia: Papúa Nueva Guinea es un país con escasos recursos y alta carga de morbilidad por tuberculosis (TB).

Objetivo: Describir las características, los desenlaces terapéuticos y los factores de riesgo de desenlaces desfavorables en los pacientes registrados para tratamiento con fármacos antituberculosos de primera línea del 1 de enero del 2014 al 31 de diciembre del 2016 en la provincia West Sepik.

Método: Fue este un estudio retrospectivo de cohortes a partir de los datos programáticos corrientes.

Resultados: De los 1058 casos, el 50,7% era de sexo masculino y el 38,8% menor de 15 años. Los casos de TB extrapulmonar correspondieron al 43,1% y 280 de los 1058 casos contaban con confirmación bacteriológica (26,5%). No se registró la situación frente al virus de inmunodeficiencia humana en el 74,7% de los

casos. De los 1019 pacientes con un desenlace registrado (96%), este fue favorable en 779 casos (76,4%) y en 240 casos fue desfavorable (23,6%). En el análisis de regresión logística multivariante, la edad se asoció con una mayor probabilidad de desenlace desfavorable (OR ajustado [ORa] 1,06 por cada aumento de 5 años; IC 95% 1,02–1,11, $P = 0,006$) y el hecho de ser un caso en retratamiento se asoció con una menor probabilidad de desenlace desfavorable, en comparación con los casos nuevos (ORa 0,54; IC 95% 0,31–0,93, $P = 0,027$).

Conclusión: En el presente estudio se encontraron deficiencias considerables en la atención de la TB como las tasas bajas de diagnóstico bacteriológico y de pruebas del VIH y las tasas altas de pérdida durante el seguimiento. Estos resultados destacan la necesidad de fortalecer las iniciativas de control de la TB, incluido el apoyo a los nuevos casos.