Short Reports

TB treatment outcomes following directly-observed treatment at an urban outpatient specialist TB facility in South Africa

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SUMMARY The treatment of 450 consecutive new patients with pulmonary TB was evaluated to determine outcome following directly-observed treatment. In all, 176 (39.1%) patients were cured, 23 (5.1%) completed treatment, 80 (17.8%) defaulted treatment, 24 (5.3%) died, 54 (12.0%) were lost to follow-up and 93 (20.7%) were transferred out. Increasing age was significant for death. Males were more likely to default and those with negative pretreatment sputum smears and those who were unemployed were more likely to be lost to follow-up. The overall treatment success rate remains low. Our data suggests that greater emphasis is needed to improve TB treatment success.

Introduction

Globally South Africa ranks seventh in terms of the TB burden.[1] In response to the growing TB burden, the South African National TB Control Programme (NTP) established standardized guidelines for TB case management, enhanced accessibility to services and adherence to treatment through the directly-observed therapy short-course (DOTS) strategy.[2,3] Despite these advances, there are wide regional variations in TB cure rates. The aim of this study was to evaluate pulmonary TB (PTB) treatment outcome following directly-observed treatment (DOT) and to identify risk factors for these outcomes.

Materials and methods

This study was conducted at the Prince Cyril Zulu Communicable Diseases Centre located in metropolitan Durban, KwaZulu-Natal, South Africa. The clinic is an outpatient specialist TB facility serving mainly the local indigent public sector users of health services. TB diagnosis and management at the clinic is in accordance with the NTP[3] and World Health Organization (WHO)[4] guidelines. Four hundred and fifty patients diagnosed and registered for PTB treatment between April and June 2001 were prospectively followed to final outcome. Patient's demographics, clinical history, sputum smear microscopy and reported chest X-ray results, TB treatment, treatment provider and treatment outcomes were assessed. Treatment outcomes[1,3,4] were categorized as cured, completed treatment, defaulted treatment, transferred out, treatment failure and lost to follow-up.[5] Data were analysed using SAS Software (SAS Institute, Inc. Carey NC). χ^2 and Fisher's exact tests were used to compare risk factors. The multinomial regression model was built, testing gender, age, direct sputum smear result and employment status with each outcome using cured as the comparison group. Relative risk was used to report the strength of the association. P values of less than 0.05 were considered statistically significant.

Results

The median age was 32 (interquartile range [IQR]: 25–40) years. The majority of the patients were men. Women were significantly younger (median age of 29.0 [IQR: 24–38] years) compared to men (median age of 33.0 [IQR: 26–41] years); ($P<0.001$). More than half (254; 56.4%) were unemployed. A previous episode of TB was reported in 24 (5.3%) patients and four (0.5%) patients reported more than one episode of TB. About one in five reported a family history of TB. The sputum smears at the first visit were positive in 292 (64.8%) with 14 (3.1%) positive at 2 months and all of those tested, negative at 6 months. In 419 (92.9%) patients, the chest X-rays were reported as active TB, with 201 (44.6%) and 108 (24.0%) showing improvement by the 2- and 6-month visit, respectively.

In all, 176 (39.1%) patients were cured, 23 (5.1%) completed treatment, 80 (17.8%) defaulted, 24 (5.3%) died, 54 (12.0%) were lost to follow-up and 93 (20.7%) were transferred out. The overall treatment success rate for the cohort was 44.2% while for sputum smear positive TB patients it was 44.8% (Table 1). In the multinomial regression analysis, increasing age (relative risk [RR] 1.3; 95% confidence interval [CI] 1.0–1.5; $P=0.004$) remained significant for death. Males were more likely to default (25.6% versus 16.9%; RR 1.9; 95% CI 1.0–3.5; $P=0.05$). The risk for loss to follow-up was higher in those with negative pretreatment direct sputum smears (25.7% versus 12.4%; RR 2.2; 95% CI 1.0–4.8; $P=0.04$) and in the unemployed (19.5% versus 9.5%; RR 2.6; 95% CI 1.2–5.3; $P=0.008$) (Table 2).

Discussion

Whilst the NTP[2,3] has enhanced its efforts towards the early detection and management of TB, the cure rate (39.1%) remains low and the default rate (17.8%) remains high. For any meaningful change to occur within the burden of TB, WHO recommends the cure rate for sputum positive cases to be greater than 85% and the

Table 1 TB treatment outcomes

Outcome	Treatment outcome			
	Sputum smear positive (n=292)		Overall (n=450)	
	n	% (95% CI)	n	% (95% CI)
Cured	128	43.8 (38.1–49.7)	176	39.1 (34.5–43.7)
Treatment completed	3	1.0 (0.2–2.9)	23	5.1 (3.2–7.6)
Treatment interruption – defaulter	53	18.2 (13.9–23.0)	80	17.8 (14.3–21.6)
Died	14	4.8 (2.6–7.9)	24	5.3 (3.4–7.8)
Lost to follow-up	32	10.9 (7.6–15.1)	54	12.0 (9.1–15.4)
Transferred out	62	21.3 (16.6–26.4)	93	20.7 (17.0–24.7)

CI, confidence interval

Table 2 Risk factors associated withTB treatment outcomes

Risk Factors	Outcome†	Unadjusted		Adjusted*		P-value
		RR	95% CI	RR	95% CI	
Age (per 5 years)	Died	1.3	1.1–1.5	1.3	1.1–1.5	0.004
	Lost to follow-up	0.9	0.8–1.0	0.9	0.9–1.0	0.07
	Defaulters	0.9	0.8–1.0	0.9	0.95–1.0	0.2
Gender (male)	Died	1.2	0.5–3.1	1.1	0.4–3.0	0.8
	Lost to follow-up	0.9	0.5–1.6	1.2	0.6–2.3	0.6
	Defaulters	1.7	0.9–2.9	1.9	1.0–3.5	0.05
Direct Sputum smear (negative)	Died	1.5	0.5–4.5	1.1	0.3–3.6	0.1
	Lost to follow-up	2.6	1.3–5.2	2.2	1.0–4.8	0.04
	Defaulters	1.0	0.5–2.2	1.0	0.5–2.3	0.9
Employment status (unemployed)	Died	1.4	0.6–3.6	1.6	0.6–4.4	0.2
	Lost to follow-up	2.7	1.3–5.3	2.6	1.2–5.3	0.008
	Defaulters	1.6	0.9–2.8	1.5	0.8–2.6	0.1

*Adjusted for risk factors listed; †Outcome: cured (includes treatment completed)
RR, relative risk; CI, confidence interval

default rate to be less than 10%. A high proportion (12%) of patients were lost to follow-up and not identified through the WHO treatment outcome criterion.[1,4] Males and the unemployed were more likely to be lost to follow-up suggesting that this group may represent a mobile population contributing to the high burden of TB often exacerbated within communities affected by poverty, poor socio-economic conditions and HIV infection.[6] While the mortality rate of 5% is perhaps a conservative estimate, defaulting and lost to follow-up patients may have contributed to the mortality. Deaths could have occurred during the early stages of diagnosis, hence the inability to trace patients and record these deaths accurately. In resource-poor countries, deaths from TB in pre-HIV era were relatively low,[7] however, the escalating burden of HIV and HIV-related TB as a complication of AIDS, has a major impact on TB transmission,[6] treatment outcome[8] and mortality rate.[8] Furthermore, our patients who died were all much younger, compared with patients from developed communities who have TB and die with advancing age. For the 20% of patients transferring out to other reporting units, we were unable to obtain information about their treatment outcome. This emphasizes the need to enhance our efforts to retain patients until completion of treatment or for a systematic referral and recording system to track such patients.

In this study, sputum smear microscopy was positive in 64.8% of patients and remains the mainstay for the diagnosis of PTB in resource-poor settings. The performance and sensitivity of sputum smear microscopy is known to decline and may have been compromised with advancing HIV disease[9] often presenting diagnostic challenges. Our data strengthens the case for the need to undertake additional research on on-site diagnosis to differentiate the reasons for the reduced sensitivity such as the low numbers of detectable bacilli in sputum specimens with advancing HIV disease. Despite the declining sensitivity of sputum smear microscopy, it remains an important tool for diagnosing the majority of cases.

This study has both strengths and limitations. The use of routinely-collected data[10] demonstrates the realities of a routine TB programme, whilst the quality of the data may be a limitation. Furthermore voluntary counselling and testing services for HIV are not routinely offered and explains the absence of any reliable estimates of TB and HIV co-infection.

Conclusion

Overall, our results demonstrate the poor treatment outcomes. Early diagnosis, reliable reporting systems for transfer-outs, procedures to prevent defaulting and more importantly those lost to follow-up need to be enhanced.

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Comparison with the Pan Malaria IgG assays for malaria diagnosis and direct microscopy among suspected malaria patients in Sanliurfa

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SUMMARY In this study, we evaluated the usage of the Pan Malaria IgG CELISA test in the diagnosis of malarial infections in Siverek-Sanliurfa, Turkey, where malarial infection is endemic and there are minimal health services available. The Pan Malaria IgG CELISA (Cellabs) test, which uses recombinant antigens and detects exposure to all four forms of malaria (*P. falciparum, P. vivax, P. ovale* and *P. malariae*) was used as individuals. Using the consensus microscopy results as the standard, sensitivity of ELISA for detection of any malarial infection in the rural populations was 83%, specificity was 85%. These results show that the performance of ELISA for the detection of any malarial infection is adequate for acute- and post-emergency situations and rural populations when the alternative is just clinical diagnosis.

Introduction

Malarial infection remains a devastating global problem, with an estimated 300–500 million cases occurring annually. Forty-one percent of the World's population live in areas where malaria is transmitted (e.g., parts of Africa, Asia, the Middle East, Central and South America, Hispaniola, and Oceania), and 700,000—2.7 million people die of malaria each year.[1,2] Malaria has the potential to be one of the important diseases in this century in Turkey.[3] There are four species causing human malaria: *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale* and *Plasmodium malaria*.[4]

In patients with malaria, a prompt and accurate diagnosis is the key to effective disease management. The gold standard test for *Plasmodium spp*. diagnosis is microscope examination of Giemsa-stained thick and thin blood smears. Although this method is a rapid and inexpensive diagnostic test, it depends on the microscopist's experience; achieving high sensitivity requires counting up to 100 microscope fields which is time-consuming and labour-intensive.[5] However, serological tests have recently been established as alternative methods to conventional microscopy for the diagnosis of malaria.[6–10] ELISA kits can detect antigen and antibody reliably and can be quite specific for malaria. To determine the diagnostic value of the Pan Malaria IgG CELISA test in this study, assay with *P. vivax* malaria patients according to clinical findings and the results of direct microscopy were utilized.

Methods

This study was undertaken in rural villages of Sanliurfa, Turkey, which is an area endemic for malaria during the period April–August 2003. Thick and thin blood films were collected from 759 people who had malaria-like symptoms such as fever and chills. Air-dried thick and thin blood films were stained with Giemsa. Stained slides were then examined under a compound light microscope using 1000x oil immersion magnification. Slides were reexamined by a second microscopist at a reference laboratory.

The Pan Malaria IgG CELISA (Cellabs Pty Ltd, Brookvale NSW, Australia) kits that we used in our study makes it possible to determinate four Plasmodium species (*P. vivax, P. falciparum, P. ovale, P. malariae*). Sera samples were kept at −80°C.

Data was collected and analysed using the SPSS (SPSS, Chicago, USA) statistical programme. For sensitivity and specificity, the test kits were compared with the microscopic results of Giemsa-stained smears. Sensitivity was calculated as the proportion of positive test results obtained among samples containing malarial parasites by microscopy; specificity was calculated as the proportion of