PREVALENCE AND PREDICTORS OF DEFAULT WITH TUBERCULOSIS TREATMENT IN SRI LANKA

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Abstract. The objectives of this study were to determine the default rate and predictors for default in patients undergoing antituberculosis treatment. All consenting patients with a confirmed diagnosis of tuberculosis admitted to a unit of the Chest Hospital, Welisara, Sri Lanka from April 2001 to April 2002 were recruited into the study. Personal and follow-up data were recorded on a pre-tested questionnaire and data sheet, respectively. A defaulter was defined as a patient who interrupted treatment for more than two consecutive months before the end of the course of treatment. Of the 892 patients recruited, 770 were new cases and 122 were relapses. The default rates were 10.3% (95% CI:8.3-12.6) and 30.3% (95% CI: 22.7-38.1) among new cases and retreatment cases, respectively, during the intensive phase of treatment and 10.9 % (95% CI:8.7-13.3) and 16.5% (95% CI:9.7-25.5), respectively, during the continuation phase. Ninety percent of new cases and 94% of retreatment cases were sputum positive for acid-fast bacilli at diagnosis. Two hundred five patients (22.9%) defaulted on treatment (95% CI: 20.3-25.8). Using logistic regression analysis, regular smokers (OR=1.9), smear positive patients who were previous defaulters (OR=2.4) and patients having involvement of less than 3 zones of the lung on chest x-ray (OR=0.5) were more likely to default compared to patients who did not smoke regularly, smear positive patients who had relapsed after taking the full course of treatment and patients with less lung involvement. Skilled and unskilled laborers were the most likely occupation to default (OR=2.03) followed by sales personnel (OR =2.00), compared to the unemployed or home-bound. A high default rate of 23% was observed among the study participants. Smoking status, occupation, history of treatment compliance of the patient, and extent of lung involvement were predictors for defaulting.

INTRODUCTION

Providing chemotherapy to all patients diagnosed with tuberculosis is the most effective strategy for preventing the spread of tuberculosis. Non-adherence to treatment has been described as an important factor in the resurgence of tuberculosis and the appearance of multi-drug resistance (Grzybowski and Enarson, 1978). In Sri Lanka, the control of tuberculosis is a major public health challenge, numbering 8,500-9,000 patients a year. Only a small increase in the number of new cases detected has been reported in the country since 1996. This may be due to improved case detection, regularization of referrals and improved notification of cases (Department of Health Services, 2002). DOTS, an internationally recommended strategy to control tuberculosis, was implemented in the country in 1997 and, at present, DOTS is in place in 23 of 26 administrative districts in the country. The National Program for Tuberculosis Control and Chest Diseases (NPTCCD) provides technical guidance for activities related to TB control in the country and functions through a network of District Chest Clinics, Branch Chest

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Clinics and Chest Hospitals/Chest Wards. The Chest Hospital situated at Welisara is the main referral center for chest diseases in the country, having 600 beds, 3 chest physicians and 2 thoracic surgeons in addition to other medical and paramedical staff.

Even with wide accessibility to free health care, default rates are high, ranging from 13% among new sputum positive cases to approximately 30% among retreatment cases (Ministry of Health, 2002). These high default rates among sputum positive patients is probably the main reason the country has not been able to achieve a decline in the number of new tuberculosis cases reported, as these treatment defaulters continue to be a source of infection to other members of the community. The purpose of this study was to identify risk factors for defaulting so the control program can adopt a strategy to manage high risk patients and decrease default rates.

MATERIALS AND METHODS

Consecutive patients fulfilling criteria for the definition of "a case of tuberculosis" (World Health Organization, 1997), resident in the Colombo and Gampaha Districts presenting to a unit at the Chest Hospital, Welisara, from April 2001 to April 2002 were recruited after obtaining informed written consent. All eligible patients consented to participate in the study included both pulmonary and extrapulmonary tuberculosis. Patients were followed up until completion of treatment or the outcome of that episode was reached. A defaulter was defined as a patient who interrupted treatment for more than two consecutive months before the end of the course of treatment.

Personal and follow-up data were recorded on a pretested questionnaire and a data sheet, respectively. WHO category 1 and 2 treatment were commenced on all new and retreatment cases, respectively (World Health Organization, 1991, 1997). Associations between defaulting and the following variables were analyzed: age, sex, occupation, family income, regular alcohol consumption, smoking, substance abuse, weight, site of lesion, type of patient, acid-fast bacillus (AFB) status in sputum, baseline chest x-ray involvement (for patients with pulmonary tuberculosis), pre-treatment serum bilirubin and alanine transaminase concentrations and development of anti-tuberculous treatment induced hepatitis.

Data were analysed using the SPSS statistical software package. Frequency distributions, chi-square tests and odds ratios were calculated. Logistic regression analyses were used to calculate adjusted odds ratios for significant variables in bivariate analyses using the probability of defaulting as the dependent variable and including an intercept in the model.

Ethical clearance was obtained from the Ethical Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura. Permission to conduct the study was obtained from the Director, Chest Hospital, Welisara, Sri Lanka. Informed consent was obtained from all participants. Participating in the study did not alter the activities of usual defaulter tracing adopted by the NPTCCD.

RESULTS

During the study period, 892 patients with confirmed tuberculosis were enrolled in the study. Of these, 205 (22.9%, 95% CI: 20.3-25.8) defaulted on treatment (Table 1). Of the 892 patients recruited, 770 were new cases and received category I treatment. The remaining 122 were retreatment cases and received category II treatment. Ninety percent of the new cases and 94% of retreatment cases were sputum positive for AFB at diagnosis.

The default rate among the new cases was slightly higher, though not significantly, during the continuation phase of treatment

(10.9%, 95% CI: 8.7-13.3) compared to the intensive phase (10.3%, 95% CI: 8.3-12.6). Among the retreatment cases, the default rate was higher, though not significantly, in the intensive phase of treatment (30.3%, 95%CI: 22.7-38.1) compared to the continuation phase (16.5%, 95% CI: 9.7-25.5) (Table 1).

A higher percentage of defaulters was seen among males (89.8%) than females (10.2%), among those 30-39 years olds (24%) compared to other age groups, those engaged in unskilled labor (40.1%) compared to other occupations and those having a family income of < Rs 5000 (39.2%) compared to higher income levels. Of the 205 defaulters, the majority consumed alcohol on a regular basis, (52.2%) were current smokers (67.3%) and were economically active (86%). Fourteen percent of the defaulters had a present or a past history of substance abuse.

Age, sex, occupational status, family income, regular alcohol consumption, current smoking status and substance abuse were independently significantly associated with defaulting ($p<0.05$) (Table 2). When the clinical profile of the patients in the two groups was considered, defaulters were significantly different ($p<0.05$) from compliers with regard to the site of lesion, type of patient, presence of AFB in the sputum and chest x-ray involvement (Table 3). The patient's weight, pre-treatment alanine transaminase and serum bilirubin concentration and the proportion of patients undergoing anti-tuberculous treatment who developed drug induced hepatitis were similar between the 2 groups (Table 3).

Binary logistic regression analyses were carried out using the probability of defaulting as the dependent variable and including significant independent predictors of defaulting described in Tables 2 and 3. Using this model, smoking status, occupation, type of patient and extent of lung involvement were predictors of defaulting (Table 4). The adjusted odds ratios were used to measure the strength of association between each independent variable and defaulting after controlling for the other variables in the model. A person who smoked regularly was 1.9 times more likely to default than a person who did not smoke regularly. A smear positive who had previously defaulted in the past was 2.4 times more likely to default again compared to a smear positive patient who had relapsed after taking the full course of treatment and was declared cured. A new patient was 0.7 times less likely to default compared to a relapsed patient. Patients having involvement of more than 3 zones of the lung on chest x-ray were 0.5 times less likely to default compared to a patient with evidence of less lung involvement. Skilled, semi-skilled and unskilled laborers were the most likely to default (OR 2.03) followed by sales personnel (OR 2.00), compared to those who were unemployed or homebound.

Table 1
Anti-tuberculous treatment default rates by treatment category and phase (*N*=892).

Phase of treatment	Default rate per 100 registered patients (95% CI)		
	New cases *n*=770	Retreatment cases *n*=122	Total *N*=892
Intensive phase, *n* (%) (95% CI)	79 (10.3%) (8.3-12.6)	37 (30.3%) (22.7-38.1)	13.0 (10.9-15.3)
Continuation phase, *n* (%) (95% CI)	75 (10.9%) (8.7-13.3)	14 (16.5%) (9.7-25.5)	11.5 (9.4-13.9)
Total treatment period, *n* (%) (95% CI)	205 (22.9%) (20.3-25.8)		

Table 2
Characteristics of defaulters and compliers with anti-tuberculous treatment.

Variable	Number (%) of		χ^2	p-value
	Treatment defaulters (*n*=205)	Treatment compliers (*n*=687)		
Age[c] (years)				
<20[a]	1 (0.5)	26 (3.8)	16.32	0.003
20-29[a]	21 (10.3)	109 (15.9)		
30-39	49 (24.0)	125 (18.2)		
40-49	56 (27.5)	153 (22.3)		
50-59	49 (24.0)	136 (19.8)		
≥60	28 (13.7)	138 (20.0)		
Sex				
Male	184 (89.8)	481 (70.0)	32.40	<0.001
Female	21 (10.2)	206 (30.0)		
Occupational status[d]				
Administrative and managerial workers[b]	0 (0)	0 (0)	70.88	<0.001
Professional, technical and related workers[b]	1 (0.5)	8 (1.2)		
Clerical and related workers[b]	0 (0)	24 (3.5)		
All other workers[b]	3 (1.5)	27 (3.9)		
Sales workers	27 (13.4)	63 (9.2)		
Skilled and semiskilled	36 (17.8)	157 (22.8)		
Unskilled	81 (40.1)	106 (15.4)		
Unemployed or retired	54 (26.7)	302 (44.0)		
Family income[e]				
< Rs 5000	60 (39.2)	153 (30.2)	4.73	0.029
> Rs 5000	93 (60.8)	353 (69.8)		
Consumption of alcohol				
Consume on a regular basis	107 (52.2)	217 (31.6)	28.51	<0.001
Others	98 (47.8)	470 (68.4)		
Smoking status				
Current regular smokers	138 (67.3)	277 (40.3)	43.58	<0.001
Others	67 (32.9)	410 (59.7)		
Substance abuse				
Having a present or a past history of substance abuse	29 (14.1)	15 (2.2)	48.13	<0.001
Others	176 (85.9)	672 (97.8)		

[a,b]Rows having the same letter were amalgamated for chi-square test.
[c]Age was not recorded in 1 patient who defaulted treatment.
[d]Occupational statuses was not reported in 3 patients who defaulted treatment.
[e]Family income was not available in 52 defaulters and 181 compliers.

DISCUSSION

In this study, the default rate of 23% is close to the rate of 27% reported from India (Chatterjee *et al*, 2003), the country with the greatest global burden of tuberculosis. In Ghana, a default rate of 13% (Dodor, 2004) was reported, and in Hong Kong the default

Table 3
Clinical profile of defaulters and compliers of anti-tuberculous treatment.

Variable	Number (%) of		χ^2	p-value
	Treatment defaulters (*n*=205)	Treatment compliers (*n*=687)		
Weight[b], kg				
<33	20 (22.2)	70 (77.8)	5.62	0.060
33-55	172 (24.3)	534 (75.7)		
>55	11 (13.0)	74 (87.0)		
Site of lesion				
Pulmonary	202 (24.4)	626 (75.6)	13.02	<0.001
Extra-pulmonary	3 (4.7)	61 (95.3)		
Type of patient				
New	154 (20.0)	616 (80.0)	43.02	<0.001
Smear positive defaulter	34 (56.7)	26 (43.3)		
Relapse [a]	13 (24.1)	41 (75.9)		
Treatment failure [a]	2 (40.0)	3 (60.0)		
Other [a]	2 (66.7)	1 (33.3)		
Sputum examination[c]				
Positive	183 (23.6)	593 (76.4)	4.43	0.035
Negative	19 (36.6)	33 (63.4)		
Chest x-ray[d]				
Involvement < 3 zones	90 (17.5)	424 (82.5)	31.12	<0.001
Involvement > 3 zones	105 (34.8)	197 (65.2)		
Serum ALT concentration prior to commencement of anti-TB treatment[e]				
≤38 IU (normal)	166 (23.3)	546 (76.7)	0.95	0.330
≥39 IU (abnormal)	35 (19.9)	141 (80.1)		
Serum bilirubin concentration prior to commencement of anti-TB treatment[f]				
≤1.1 mg/dl (normal)	198 (22.5)	682 (77.5)	2.44	0.118
≥1.2 mg/dl (abnormal)	4 (44.4)	5 (55.6)		
Anti-tuberculous treatment induced hepatitis				
Yes	13 (17.6)	61 (82.4)	1.34	0.248
No	192 (23.5)	626 (76.5)		

[a] Amalgamated as numbers were small.
[b]Weights of 2 defaulters and 9 treatment compliers were not recorded.
[c]Sputum examination results are for patients having pulmonary TB.
[d]Chest x-rays were not available in 7 defaulters and 5 treatment compliers with pulmonary TB.
[e]Serum ALT (alanine transaminase) concentrations were not available in 4 defaulters.
[f] Serum bilirubin concentrations were not available in 3 defaulters.

rate was 8% (Chan-Yeung *et al*, 2003). Both these figures are considerably lower than those found in our study. From a control program perspective, this default rate is unacceptably high. A limitation of this study was the inability to follow up the defaulters individually to see the outcome of the event as they may have sought treatment from another government or a private health care facility. This is a rare possibility, since we enrolled only

Table 4
Summary of logistic regression analysis using default status as the dependent variable.

Variable	Coefficient	p-value	Odds-ratio	95% CI of odds-ratio
Intercept	-1.242			
Current regular smoker[a]	0.622	0.002	1.863	1.267 - 2.738
Type of patient[b]		<0.001		
New patient	-0.403	0.259	0.668	0.332 - 1.345
Smear positive defaulter	0.892	0.043	2.441	1.030 - 5.782
Chest x-ray involvement > 3 zones[c]	-0.713	<0.001	0.490	0.344 - 0.699
Occupation[d]		0.006		
Professional, technical and clerical	-5.147	0.515	0.006	0.00 - 310.272
Sales personnel	0.697	0.022	2.007	1.105 - 3.643
Skilled/semi skilled and unskilled laborers	0.710	0.001	2.033	1.351 - 3.060

[a]Reference group are those who do not smoke on a regular (1 or more cigarettes daily) basis.
[b]Reference group are patients who have relapsed with smear positive TB after taking the full course of treatment and declared cured.
[c]Reference group are those with chest x-ray involving less than 3 zones of the lung.
[d]Reference group are those who are unemployed or home-bound.

the patients who resided in the Colombo and Gampaha Districts for which the Chest Hospital, Welisara was not only the most centrally located health facility providing tuberculosis treatment but also the center conventionally regarded as having the most efficacious treatment for tuberculosis by the general public.

Ninety percent of the new and re-treatment cases were sputum positive for acid-fast bacilli at the time of diagnosis. These patients constitute an important reservoir of infection. Among the retreatment cases, a high default rate was seen during the intensive phase of treatment compared to the continuation phase of treatment or in new cases. In addition to being a source of infection in the community, defaulting among retreatment cases favors selection of multi-drug resistant strains. Hence, when restarting treatment on a patient who has defaulted previously, the importance of compliance with treatment for the required duration should be emphasized. In these patients, close follow-up by obtaining extra support from the local health care facility may be beneficial.

In this study age, sex, occupational status, family income, regular alcohol consumption, current smoking status and substance abuse, were significantly associated with treatment default. However, on multivariate analysis, the type and extent of lung involvement, smoking status, and occupation were significant predictors of defaulting. Some variables that were independently associated with default status were excluded from the multivariate model due to associations between independent variables.

Based on the multivariate model, patients who defaulted on treatment previously, whose extent of lung involvement was less, who smoked, or who were engaged in certain occupations were more likely to default. On bivariate analysis chest x-ray evidence of more lung involvement favored defaulting. On multivariate analysis, when the effects of other confounding variables were adjusted for, those having >3 zones of lung involvement were less likely to default than those with less lung involvement. This is probably due to the asso-

ciation between lung involvement and other variables, such as previous defaulting. Subjects with less lung involvement were more likely to improve more quickly and hence default on treatment earlier. Hence, it is important education programs target this particular group of patients.

Although gender was a significant predictor of defaulting independently, on the multivariate model it was not significant, possibly because the majority of subjects were males and gender being associated with other variables. Reasons for males defaulting more than females may be due to males being the main income source among families in this part of the world. Illness of this nature prevents them from engaging in their routine income generating work, mostly in the informal sector, and thus reducing family income. The default rate was also high among those doing unskilled labor, a group that does not have a regular income unless they work. Males are more likely to adopt unhealthy practices, such as consuming alcohol and smoking tobacco and may be more likely to default treatment. In such cases, community based treatment programs, where the health worker visits the patient or a reliable relative observes the patient and makes sure that the patient takes the treatment, should be adopted to improve compliance with treatment.

This study identified important risk groups that should be targeted for educational programs and closely monitored after commencing treatment. Custom made DOTS strategies should be developed for these patients. Involvement of the family early in treatment should be given consideration if we are to improve compliance in these patients.

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