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Kimberly A. D'Souza

Interactive Research & Development, Karachi, Pakistan

Syed M A. Zaidi

Community Health Solutions, Karachi, Pakistan

Maria Jaswal

The Indus Hospital, TB Program, Karachi, Pakistan

Shahid Butt

The Indus Hospital, TB Program, Karachi, Pakistan

Saira Khowaja

Interactive Research & Development, Karachi, Pakistan

See next page for additional authors

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Authors

Kimberly A. D'Souza, Syed M A. Zaidi, Maria Jaswal, Shahid Butt, Saira Khowaja, Shifa Salman Habib, and Aryn A. Malik



Short Report

Factors associated with month 2 smear non-conversion among Category 1 tuberculosis patients in Karachi, Pakistan



Kimberly A. D'Souza^a, Syed M.A. Zaidi^b, Maria Jaswal^c, Shahid Butt^c, Saira Khowaja^a, Shifa S. Habib^{b,*}, Aryn A. Malik^a

^a Interactive Research & Development, 1-A, North Park Street, Phase 1, Defence Housing Authority, Karachi, Pakistan

^b Community Health Solutions, Suite 508, Ibrahim Trade Tower, Main Shahrah-e-Faisal, Karachi 75300, Pakistan

^c The Indus Hospital, TB Program, Plot C-76, Sector 31/5, Opposite, Korangi Crossing Rd, Karachi, Pakistan

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ABSTRACT

Predictors of smear non-conversion at baseline can help identify cases at risk for failure of tuberculosis treatment. Retrospective data for smear-positive Category 1 patients in Karachi, Pakistan, was analyzed. Predictors of sputum conversion were determined using multiple logistic regression with sputum conversion as outcome variable and patient demographics, baseline weight, baseline sputum smear grade, case-finding approach as explanatory variables. Age ≥ 35 years, baseline sputum grade of 3+ were significantly associated with predicting sputum smear positivity at month 2 of treatment. Monitoring compliance to TB treatment should be considered amongst older patients and those with a high sputum grade at baseline.

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Introduction

Pakistan has the fifth highest burden of tuberculosis globally [1]. Of the estimated 510,000 new Tuberculosis (TB) cases, only 65% were notified to the National Tuberculosis Program (NTP) in 2015, and increasing case-notifications is a key priority [1]. In high TB-burden countries like Pakistan, ensuring treatment compliance and achieving a high treatment success rate therefore often receives less attention [2]. In addition, limited resources prevent stringent community-based monitoring of detected cases. In such settings, identifying patients at high-risk for treatment failure and dedicating resources to ensure treatment compliance has been recommended [3]. Patients observing compliance to TB medication should convert after 2 months of treatment [4]. However, even though patients self-report a high compliance, the proportion of TB patients that remain smear-positive after 2 months can be as high as 20% [3,5,6]. Sputum smear positivity at month 2 of treatment has been identified as an important predictor of treatment failure [4,5,7].

The aim of this study was to determine risk-factors at baseline that contribute to failure of smear-conversion at month 2 of treatment among bacteriologically positive Category I (treatment-naive), pulmonary TB patients diagnosed in Karachi, Pakistan.

Patients and methods

We abstracted retrospective data of patients registered at the TB clinic of The Indus Hospital, a large tertiary care facility in Korangi Town, Karachi, Pakistan, between January 2007 and December 2013. Participants included Category I smear positive cases older than 15 years with a follow-up sputum smear result at month 2 of treatment. Despite, the hospital having a rigorous protocol for sputum expectoration, using nebulizers and mucolytic agents, a total of 1312 cases could not have a follow-up sputum smear and were excluded from the analysis. Patient demographic and clinical data were obtained from the hospital records. All patients received standardized TB regimens in accordance with the NTP guidelines. Smear microscopy for diagnosis and follow-up was performed using Ziehl-Neelsen staining methods.

Ethics approval

The study was approved by Institutional Review Board (IRB) at Interactive Research and Development (IRD), Karachi, Pakistan. The IRB is registered with U.S. Department of Health and

* Corresponding author.

E-mail addresses: kimberly.dsouza@irdresearch.org (K.A. D'Souza), asad.zaidi@chshealthcare.org (S.M.A. Zaidi), maria.jaswal@industbcontrol.org (M. Jaswal), shahid.butt@industbcontrol.org (S. Butt), saira.khowaja@irdresearch.org (S. Khowaja), shifa.habib@chshealthcare.org (S.S. Habib), amryn.malik@irdresearch.org (A.A. Malik).

Table 1
Baseline characteristics of Category I TB patients enrolled for treatment at The Indus Hospital TB Program, Karachi, Pakistan (January 2007 – December 2013).

	Mth 2 Pos, n (%) 377 (19.5)		Mth 2 Neg, n (%) 1561(80.5)		Total, n (%) 1938	
Gender						
Male	192	50.9%	708	45.4%	900	46.4%
Female	185	49.1%	853	54.6%	1038	53.6%
Age						
15–34 years	230	61.0%	1051	67.3%	1281	66.1%
≥35 years	147	39.0%	510	32.7%	657	33.9%
Weight						
<30	12	3.2%	29	1.9%	41	2.1%
30–39.5	95	25.2%	367	23.5%	462	23.8%
40–54.5	202	53.6%	880	56.4%	1082	55.8%
55+	68	18.0%	285	18.3%	353	18.2%
Baseline sputum grade						
Scanty (1–9 AFB)	12	3.2%	171	11.0%	183	9.4%
1+	74	19.6%	570	36.5%	644	33.2%
2+	96	25.5%	368	23.6%	464	23.9%
3+	195	51.7%	452	29.0%	647	33.4%
Approach of case-detection						
Facility-based (passive)	208	55.2%	781	50.0%	989	51.0%
Community-screening (active)	169	44.8%	780	50.0%	949	49.0%
Outcomes						
Success (cured + completed)	291	77.2%	1405	90%	1696	87.5%
Failure	46	12.2%	25	1.6%	71	3.7%
Default	30	8.0%	101	6.5%	131	6.8%
Died	3	0.8%	13	0.8%	16	0.8%
Transfer out	7	1.9%	16	1.0%	23	1.2%
Diagnosis changed	0	0.0%	1	0.1%	1	0.1%

Human Services (DHHS), Office for Human Research Protections (IRB#00005148).

Statistical analysis

Statistical analyses were carried out using Stata/IC 12 (College Station, TX: StataCorp LP). Frequency analysis of demographics and baseline clinical characteristics was performed. Predictors of sputum conversion were determined using bi-variate and multiple logistic regression with sputum conversion as the outcome variable and patient demographics, baseline weight, baseline sputum smear grade and case-finding approach as the explanatory variables. Age and weight were included as categorical variables in the model. Adjusted analyses were subsequently performed through backward step-wise logistic regressions using Akaike's Information Criteria (AIC) to select the final model. The regression model was assessed for goodness-of-fit using Hosmer–Lemeshow goodness-of-fit test. Multi-co-linearity within the explanatory variables was assessed using Variance Inflation Factor (VIF). Differences in baseline characteristics between patients with Month 2 sputum sample compared to those without sample were analyzed using χ^2 statistic.

Results

A total of 1938 patients diagnosed with Category I, pulmonary TB were included in the analysis, of which 900 (46.4%) males and 1038 (53.6%) females (Table 1). A majority of the patients were aged 15–34 years (66.1%). A total of 377 (19.5%) patients were smear-positive at month 2 of treatment, 51.7% of which had a baseline sputum grade of 3+.

The overall treatment success rate for the study population was 87.5%, of which 52.3% patients had been cured and 35.2% had completed the treatment regimen. Treatment success rate for cases that were smear-positive at month 2 compared to those that were negative was 78.6% and 90% respectively. A treatment failure rate of 3.7% was recorded.

Age greater than or equal to 35 years (aOR, 1.33, 95% CI: 1.05–1.69) and baseline sputum grade of 3+ (aOR 6.21, 95% CI: 3.37–11.41) were significantly associated with predicting sputum smear positivity (Table 2). Gender, baseline weight and approach of case-detection were not associated with sputum smear positivity at month 2.

Discussion and conclusion

Similar to reported literature, our study found a high proportion (19.5%) of cases with positive month 2 smear. Previous studies have identified male sex, older age, higher baseline sputum grade, smoking habits and extensive disease involvement on chest X-ray as determinants of persistent smear-positivity at the end of intensive phase of treatment [3,5–9]. Our results support existing evidence indicating association of older age and high sputum grade with adverse sputum-conversion outcomes in the Pakistani population [10]. Early identification of such high-risk patients and intensive follow-ups are not routinely practiced by TB programs, who can benefit from counseling sessions and strict monitoring of treatment compliance during intensive phase of treatment [2]. Ensuring treatment compliance is critical to maintaining effectiveness of a treatment program which is the “cornerstone” for reducing TB transmission [11]. Other innovative approaches, such as, SMS reminders and conditional-cash transfers for adherence to treatment regimens may be considered for implementation at a programmatic level, tailored for patients at high-risk for treatment failure [12].

Further research, using provincial and national programmatic data, is required to validate these findings and draw relevant recommendations for TB treatment facilities in low-income, high burden countries. In addition, further studies are recommended, using Xpert MTB/RIF as the baseline diagnostic test to assess presence of similar associations between sputum conversion and treatment outcomes, with semi-quantitative MTB burden result provided by Xpert MTB/RIF testing on Rif-susceptible patients.

Table 2
Determinants of Month 2 sputum conversion amongst patients enrolled at The Indus Hospital TB Program, Karachi, Pakistan (January 2007 – December 2013).

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-Value (Adjusted OR)*
Gender			
Male	Ref	–	
Female	1.28 (1.00–1.57)	–	
Age			
15–34 years	Ref	Ref	
≥35 years	1.35 (1.04–1.73)	1.33 (1.05–1.69)	0.02
Baseline sputum grade			
Scanty (1–9 AFB)	Ref	Ref	
1+	1.83 (0.96–3.44)	1.86 (1.00–3.52)	0.063
2+	3.64 (1.94–6.83)	3.73 (1.99–6.98)	<0.01
3+	5.96 (3.23–10.97)	6.21 (3.37–11.41)	<0.01
Weight			
<30 kg (ref)	Ref	–	
30–39 kg	1.15 (0.69–1.92)	–	
40–54 kg	0.98 (0.61–1.56)	–	
≥55 kg	0.80 (0.50–1.30)	–	
Approach of case-detection			
Facility-based (passive)	Ref	–	
Community- screening (active)	0.81 (0.65–1.02)	–	
Hosmer–Lemeshow χ^2 p-value	0.39	0.11	

Our study was limited by number of variables explored due to reliance on quarterly programmatic data being reported to NTP by the Indus Hospital. Other variables that may predict treatment outcomes need to be considered such as severity of disease on radiological investigations. We were unable to adjust for BMI since patient heights are not recorded during surveillance of TB outcomes. There may be potential for selection bias as despite rigorous protocols, cases which could not expectorate a follow-up sputum sample were excluded. Due to limited availability of rapid diagnostic tests during the study period, primary Drug Susceptibility Testing (DST) could not be carried out. Further studies are needed that have excluded the possible effect of drug resistance on treatment outcomes.

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Competing interests

None declared.

Ethical approval

Not required.

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