Factors affecting defaulting from DOTS therapy under the national programme of tuberculosis control in Alexandria, Egypt

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العوامل المؤثِّرة على إخفاق المعالجة القصيرة الأمَد تحت الإشراف المباشر (دوتس) ضمن البرنامج الوطني لمكافحة السل في الإسكندرية، مصر

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الخلاصة: تهدف هذه الدراسة للحالات والشواهد غير المتوافقة إلى التعرُّف على العوامل المؤثِّرة في الإخفاق في المعالجة ضمن البرنامج الوطني لمكافحة السل في الإسكندرية، مصر، وقد أجرَى الباحثون مراجعات للسجلات ومقابلات منظّمة مع 53 من الذين أخفقت معالجتهم، ومع 187 من الشواهد الذين اختاروهم عشوائياً. وأوضح التحليل الوحيد المتغيِّر أن 13 عاملاً من بين 54 عاملاً استقصاها الباحثون قد ترابطت ترابُطاً يُعْتَدُّ به إحصائياً مع الإخفاق، وبعد إجراء التحوف اللوجستي التدريجي، بقيَت خمسة عوامل في النموذج، وهي: العمر الأصغر (معدل الأرجحية 0.16)، والإقامة في منطقة ريفية (معدل الأرجحية 12.9)، وأوقات الانتظار الطويلة (معدل الأرجحية 5.81)، وسوء التواصل بين المريض والطبيب (معدل الأرجحية 3.06)، والخوف من تسرُّب المعلومات (معدل الأرجحية 3.62). أما الأسباب التي ذكرها الذين أخفقت معالجتهم فتشمل المسافة الطويلة للوصول إلى العيادة، وعدم ملاءمة أوقات العيادات، وأوقات الانتظار الطويلة. أما العوامل الرئيسية للإخفاق في البرنامج الوطني لمكافحة السل في الإسكندرية، مصر فقد كانت عوامل تتعلق بالخدمة، وهي عوامل يمكن تصحيحها وتحسينها.

ABSTRACT This unmatched case–control study aimed to identify factors affecting default from therapy under the national programme of TB control in Alexandria, Egypt. Record reviews and structured interviews were made with 57defaulters and 187 randomly selected controls. Univariate analysis showed 13 out of 54 factors investigated were significantly associated with defaulting and, after stepwise logistic regression, 5 factors remained in the model: younger age (adjusted OR= 0.16), rural area of residence (OR = 12.9), long waiting times (OR = 5.81), poor physician–patient communication (OR = 3.06) and fear of information leakage (OR = 3.62). Reasons cited by defaulters included long distance to the clinic, unsuitable clinic times and long waiting times. The main factors associated with defaulting from the national programme of TB control in Alexandria, Egypt were service-related factors, which are amenable to improvement.

Facteurs liés à l'abandon du traitement DOTS dans le cadre du programme national de lutte antituberculeuse à Alexandrie (Égypte)

RÉSUMÉ La présente étude cas-témoins non appariés visait à identifier les facteurs influant sur l'abandon du traitement dans le cadre du programme national de lutte antituberculeuse à Alexandrie (Égypte). Les dossiers médicaux de 57 patients ayant abandonné le traitement et de 187 témoins sélectionnés aléatoirement ont été examinés puis des entretiens structurés ont été menés. Une analyse univariée a démontré que 13 facteurs étudiés sur 54 étaient significativement associés à un abandon et, après une analyse de régression logistique par étapes, cinq facteurs ont été dégagés à partir du modèle : un âge plus jeune (OR ajusté = 0,16), un lieu de résidence en milieu rural (OR = 12,9), un long temps d'attente (OR = 5,81), une mauvaise communication entre le médecin et le patient (OR = 3,06) et la crainte de la divulgation d'informations (OR = 3,62). Une longue distance pour atteindre l'établissement de soins, des horaires d'ouverture peu pratiques et de longs temps d'attente comptaient parmi les raisons citées par les patients ayant abandonné le traitement. Les principaux facteurs associés à un abandon du traitement dans le cadre du programme national de lutte antituberculeuse à Alexandrie (Égypte) relevaient du domaine des services se prêtant aux améliorations.

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Introduction

Despite being a curable disease tuberculosis (TB) remains a serious public health problem in Egypt, as it is worldwide [1–3]. Revised estimate of TB incidence in Egypt published by the World Health Organization (WHO) in 2009 reported 21 cases per 100 000 population per annum. Of these cases 9 per 100 000 were sputum-positive, which is the most dangerous source of infection [4]. After establishment of the national TB control programme in Egypt (NTP-Egypt) [5], the country has succeeded in meeting the World Health Organization's global targets. In 2009 the case detection rate of positive cases in Egypt was 72% (global target is 70%) and treatment success rate was 87% (global target is 85%) [4].

A major contributor to both treatment failure and the rise of multidrug-resistant TB is inadequate and incomplete treatment [6]. Default is defined by the WHO as treatment interruption of 2 consecutive months or more, and is often used synonymously with drop-out from treatment before completion [7]. In 1996, the NTP-Egypt took action to tackle low adherence to TB treatment and began implementation of the DOTS programme [8]. After this the situation improved; official data published by NTP-Egypt showed that the average rate of defaulting in Egypt in 2008 was 4% and that Alexandria governorate had the same rate as the national average (4%) [9].

Factors affecting the rate of default among TB patients have been studied in countries other than Egypt and it seems that variables associated with defaulting from TB programmes differ according to the characteristics of the setting. Studies in Brazil, South Africa, Russia and Thailand showed that significant factors included socioeconomic (unemployment, monetary resources, homelessness, history of imprisonment), clinical (side-effect, alcoholism, use of illegal drugs, HIV infection) and service-related (long waiting times for a consultation, transportation difficulties to the service) [1,2,10,11]. Several studies have identified that quality of communication between patients and health care workers is also an important motivating factor for completion of treatment [12–14]. The present study aimed to identify factors affecting defaulting from DOTS therapy among Egyptian TB patients in Alexandria who started their anti-TB treatment under the NTP-Egypt.

Methods

Study design and sample

The study was conducted at 7 government-run chest disease dispensaries belonging to 6 districts in Alexandria, under the control of Egypt Health Affairs. At the start of the study in January 2010, the total number of patients on the TB registries of these dispensaries was 564. An unmatched case–control study design was used. Cases (defaulters) were defined as patients who had failed to collect medication for more than 2 consecutive months after the date of the last attendance during the course of treatment [14]. Controls (non-defaulters) were defined as patients who continued their treatment without defaulting during the past 3 months.

All defaulters were recorded in a specially designed register. The total number of defaulters at the start of the study was 57; all of them were included in the study. Owing to the small number of cases, an unequal sample size design was selected with a ratio of 3 cases to 10 controls. The sample size was calculated based on the assumption that unemployment is an important risk factor for default. The sample size was calculated using the Fleiss formula with continuity correction factor [15]. Assuming an odds ratio of 2.5, and unequal sample size of cases and controls (ratio of 1:3), a sample size of 57 cases and 187 controls was required to demonstrate with 95% certainty and with a power of 80% that unemployment was a statistically significant risk factor for default. To select controls, a systematic random sample was used to select patients from the register of TB patients who attend to collect their treatment. Every second patient was selected to complete the sample size of controls (187 controls) [16].

Data collection

Data collection lasted from 1 February to 30 April 2010. Data were collected using a structured interview in Arabic language and a record review. The interview was developed by the researchers based on a literature review of factors affecting defaulting among TB patients. A pilot study was carried out and 2 items were added based on its results. The total number of investigated factors included in the final version of the interview schedule was 54. The following factors were included in the analysis:

- *Sociodemographic and economic factors.* age; sex; marital status; education; residence; crowding index; monthly income; household possessions; owing a private house.
- *History and habits.* Period between symptoms and start of treatment; BCG vaccination; exposure to other TB patients; smoking; alcohol intake.
- *Signs and symptoms.* General weakness; loss of appetite; loss of weight; low-grade fever; night sweating; severe cough for 2 weeks or more; haemoptysis; chest pain; sputum examination result.
- *Patient's knowledge.* Disease signs and symptoms; methods of disease transmission; duration of TB treatment.
- *Facility-related factors.* Convenience of clinic hours; waiting time; convenience of waiting place; getting medications from different dispensary than that of initial diagnosis; availability of transportation to dispensary; transportation cost; travelling time to dis-

pensary; frequency of physician visits; physician tells patient about next visit date; rapport between clinic staff and patients; respect and caring by physician; any monetary payments at the clinic; provision of initial medical examination on first contact; provision of medical examination at each encounter.

- *Physician–patient communication.* Physician listens to patient complaints; explains the current medical condition; explains the expected complications; explains the duration of treatment; explains the expected complications of treatment; explains the results of investigations.
- *Other factors.* Availability of home care; availability of emotional support; patient's feeling of improvement with treatment; patient's belief that TB is not a curable disease; patient being ashamed of the disease; patient's belief that DOTS represents a burden of any kind; patient's fear of information leakage; patient's acceptance of medications (taste, size of tablets, number of tablets).

At the end of the interview defaulters were asked to list the most important reasons for defaulting from the programme using an open-ended question.

Defaulters were approached by one of the researchers and each social worker at the 7 chest diseases dispensaries. Interviews were conducted at the patient's home or one of the dispensaries. Controls were interviewed when they attended to collect their treatment. Following patients' interviews a review was made of medical records of both cases and controls to collect clinical data such as date of starting treatment and initial symptoms. In addition, social worker records were reviewed to collect sensitive sociodemographic data such as income and housing condition.

Consent was taken from each patient before participation. Patient identification data were kept confidential.

Statistical analysis

Statistical analysis was carried out using *SPSS*, version 16. Pearson chi-squared test was carried out to assess the association of different factors with defaulting from TB treatment. In case of sparse data, the Fisher exact probability was used as indicated. Unadjusted odds ratio (OR) and confidence intervals (CI) were presented to illustrate the magnitude of effect of different factors on defaulting from TB treatment. Significant factors in univariate analysis were included in a stepwise logistic regression analysis. The model fit was assessed using the omnibus test of model coefficients. It tests if the model with the predictors is significantly different from the model with only the intercept. Two-tailed *P*-value was reported and statistical significance was established at $P < 0.05$.

Results

Univariate analysis

Out of 54 investigated factors, only those that had significant associations with defaulting from NTP-Egypt are presented here. Table 1 shows that 2 sociodemographic factors (age and

Table 1 Univariate analysis of sociodemographic and clinical factors associated with defaulting from tuberculosis treatment

Sociodemographic and clinical factors	Defaulters (*n* = 57)		Non-defaulters (*n* = 187)		*P*-value	OR (95% CI)
	No.	%	No.	%		
Age (years)						
< 30[a]	13	22.8	31	16.6		
30–	16	28.1	64	34.2	0.03	0.60 (0.26–1.39)
40–	20	35.1	39	20.9		1.22 (0.53–2.84)
50 +	8	14.0	53	28.3		0.36 (0.13–0.97)
Area of residence						
Urban[a]	22	38.6	143	76.5		
Squatter	24	42.1	41	21.9	< 0.001	3.80 (1.94–7.47)
Rural	11	19.3	3	1.6		23.8 (6.15–92.2)
Period between symptoms & treatment (weeks)						
1–3[a]	27	47.4	128	68.5		
4+	30	52.6	59	31.5	0.004	2.41 (1.32–4.41)
Cough						
Mild or moderate[a]	1	1.8	23	12.2		
Severe	56	98.2	164	87.8	0.02	7.85 (1.04–59.5)

[a]*Reference category.*
OR = odds ratio; CI = confidence interval.

area of residence) were significantly different between defaulters and non-defaulters using univariate analysis. A higher percentage of defaulters than non-defaulters were found among patients aged < 30 years (22.8% and 16.6% respectively). The highest percentage of defaulters (42.1%) lived in squatter areas, while most of the controls (76.5%) lived in urban areas. When compared with patients residing in the urban area, patients living in the rural area were 23.8 times more likely to default while those living in a squatter area were 3.8 times more likely to default than those living in urban areas.

Significant clinical factors included the period between symptoms and treatment and severity of cough. Patients with a long duration between symptoms and start of treatment were 2.41 times more likely to default than patients with a short duration between symptoms and start of treatment. Patients presented with severe cough were 7.85 times more likely to default from treatment than those presenting with mild or moderate cough.

Factors related to the health service, including facility-related factors and physician–patient communication, were compared between defaulters and non-defaulters. Patients who reported unsuitable clinic opening times and long waiting times were more likely to default (OR = 9.33 and OR = 4.33 respectively). Three significant physician–patient communication factors were identified (Table 2). Defaulting from the national programme of TB control was more likely to occur among patients who reported "physicians don't listen to complaints" (OR = 16.3), "physicians don't explain TB complications" (OR = 3.55) and "physicians don't explain treatment side-effects" (OR = 6.65).

Significant patient perception factors are illustrated in Table 3. Patients who did not feel better with treatment and who had a negative perception of the ability of TB treatment to completely cure the disease defaulted more than those who answered positively to both questions (ORs = 4.82 and 11.5 respectively). Patients feeling shame about TB and patients fearing information leakage were more likely to default than those who answered negatively to both questions (ORs = 0.45 and 0.39 respectively).

Multivariate regression analysis

Using univariate analysis significant factors associated with defaulting from TB treatment (13 factors) were included in a stepwise multivariate logistic regression. Owing to the presence of multicolinearity between 3 significant factors measuring physician–patient communication [variance inflation factor (VIF) > 2.5], these variables were combined into a single variable (physician–patient communication). Out of 11 investigated variables, 5 variables remained in the last step: age group, area of residence, long waiting times, poor physician–patient communication and fear of information leakage (Table 4). Patients aged 50+ years were 6 times less likely to default from TB treatment than patients aged < 30 years (adjusted OR = 0.16, 95% CI: 0.03–0.46). Patients who lived in rural areas showed the highest likelihood of defaulting from TB treatment (adjusted OR = 12.9). Patients who feared information leakage and reported poor physician–patient communication were 3 times more likely to default from TB treatment (adjusted ORs = 3.62 and 3.06 respectively).

Defaulters' reported reasons

Defaulters reported one or more reasons for defaulting from the TB DOTS programme, amounting to a total of 135 reasons. Unsuitable opening time at the clinic was the most frequently cited reason for defaulting, accounting for over a quarter of the reasons (28.2%). The next most common reasons were the distance of clinic from home, long waiting times before examination and being unaware of the need to complete the

Table 2 Univariate analysis of health service factors associated with defaulting from tuberculosis (TB) treatment

Service factors	Defaulters (*n* = 57)		Non-defaulters (*n* = 187)		*P*-value	OR (95% CI)
	No.	%	No.	%		
Facility						
Unsuitable clinic times	21	36.8	11	5.9	0.001	9.33 (4.14–21.0)
Long waiting times	36	72.2	53	28.3	0.001	4.33 (2.32–8.10)
Physician–patient communication						
Physicians don't listen to complaints	15	26.3	4	2.1	< 0.001	16.3 (5.16–51.8)
Physicians don't explain TB complications	6	10.5	6	3.4	0.04	3.55 (1.10–11.5)
Physicians don't explain treatment side-effects	15	26.3	10	5.3	< 0.001	6.65 (2.65–15.1)

OR = odds ratio; CI = confidence interval.

Table 3 Univariate analysis of patient perception factors associated with defaulting from tuberculosis treatment

Patient perceptions	Defaulters (*n* = 57)		Non-defaulters (*n* = 187)		*P*-value	OR (95% CI)
	No.	%	No.	%		
Felt better with treatment						
Yes[a]	41	71.9	173	92.5		
No	16	28.1	14	7.5	< 0.001	4.82 (2.18–10.7)
Treatment cured TB completely						
Yes[a]	48	84.2	184	98.4		
No	9	15.8	3	1.6	< 0.001	11.5 (2.99–44.1)
Feel shame about TB						
Yes[a]	43	75.4	108	57.8		
No	14	24.6	79	42.2	0.02	0.45 (0.23–0.87)
Fear of information leakage						
Yes[a]	35	61.4	72	48.5		
No	22	38.6	115	61.5	0.002	0.39 (0.21–0.72)

[a]*Reference category.*
OR = odds ratio; CI = confidence interval.

treatment; each accounted for 12.6%. Feeling better after initial treatment ranked third (11.9%).

Discussion

Failure to complete the treatment regimen has historically been cited as one of the most challenging problems in TB treatment. The aim of this study was to investigate possible factors affecting patients' defaulting from the NTP-Egypt DOTS programme at government chest dispensaries in Alexandria, Egypt. The study investigated 54 factors that might affect defaulting. Stepwise multivariate logistic regression analysis revealed 5 significant factors, including younger age, living in a squatter or rural area, long waiting times, poor physician–patient communication and patients' fear of information leakage.

Younger patients aged < 30 years were 6.25 times more likely to default than patients aged 50+ years. A effect of age on defaulting was reported in a study conducted in Russia where defaulting was associated with age < 45 years [17].

Patients residing in rural and squatter areas had a significantly higher likelihood of defaulting, especially those residing in rural areas, who showed the highest adjusted odds ratio (OR = 12.9). Profiles of high-burden countries showed that the public health care systems, into which TB control is fully integrated, are constrained by a lack of human resources and difficulties in providing outreach services. This is particularly the case in rural areas in countries such as Ethiopia, Indonesia, Nigeria and Pakistan [4]. Expansion of the network of general health care facilities will improve access to health care and ultimately help to achieve targets for TB control [4]. The WHO report published in 2006 on enhancing the DOTS programme indicated that particular attention should be given to the poorest and most vulnerable population groups [18].

Factors related to the health services were found to be important variables associated with defaulting from DOTS. Facility-related factors, namely unsuitable clinic hours and long waiting times, were significantly associated with defaulting. Similar results were reported in a study conducted in Brazil in 2004, which reported long waiting times for a medical consultation as an associated factor for defaulting from treatment [1]. Reasons cited for defaulting by our cases showed the importance of facility factors such as unsuitable clinic times and long waiting times before examination. Problems with physician–patient communication were also found to have a negative impact on continuation of TB treatment. Out of 6 factors related to physician–patient communication, 3 communication factors were found to be statistically significant: physicians not listening to complaints, physicians not explaining TB complications and physicians not explaining treatment side-effects. Patients reporting poor physician communications were 3 times more likely to default from TB treatment (adjusted OR = 3.06). Patients typically default when they experience improvement of symptoms with treatment, while unawareness of the side-effects of medication can be misinterpreted by patients as drawbacks of treatment. The relationship between medication side-effects and treatment defaulting has been frequently demonstrated in other studies [3,10,19–21]. It has been recommended that health care staff in TB programmes should direct health education towards expected side-effects of treatment. Nurses should teach patients to recognize and manage severe

Table 4 Multivariate logistic regression analysis of factors associated with defaulting from tuberculosis treatment

Factors	Adjusted OR (95% CI)	*P*-value
Age (years)		
< 30[a]		
30–	0.71 (0.24–2.11)	0.53
40–	0.57 (0.20–1.66)	0.30
50 +	0.16 (0.03–0.46)	0.002
Area of residence		
Urban[a]		
Squatter	2.74 (1.12–6.73)	0.027
Rural	12.9 (2.53–65.7)	0.002
Long waiting times	5.81 (1.80–18.8)	0.003
Poor physician–patient communication	3.06 (1.02–9.46)	0.049
Fear of information leakage	3.62 (1.54–8.53)	0.003

[a]*Reference category.*
OR = odds ratio; CI = confidence interval.

medication side-effects and request patients to schedule an extra clinic visit if they experience side-effects in order to reduce treatment defaulting [10].

Several patient perception factors were investigated in the present study, many of which were significant in univariate analysis. Although multivariate analysis revealed only 1 factor related to patient perceptions, it is important to discuss these factors as they are amenable to improvement at a lower cost to the community. Lack of improvement with treatment and patients' perception that treatment cannot cure TB completely were significantly associated with defaulting. These findings are in agreement with a study conducted in Russia in 2008, which indicated that non-adherent patients did not believe that they will fully recover and thus did not want to continue treatment [17]. An association between patients' knowledge about the duration of treatment and treatment adherence has also been shown in other studies [3,17,20,22–24]. The present study showed that most of the defaulters were ashamed of their disease and concerned about leakage of information. Stigmatization of TB leads to a situation where many patients are not treated well by members of the community. The stigma associated with TB has been shown to have a significant effect on defaulting from treatment [17,25]. TB treatment polices must address confidentiality of information about patients' private data. Patients should be assured about the confidentiality of their information to ensure their compliance with attendance.

There are a number of limitations in the present study that affect the generalizability of the results. The small number of cases increased the value of each case and may have exaggerated some factors. Moreover, the study was conducted only in chest dispensaries of Alexandria governorate. Despite similarities between TB patients living in different governorates all over Egypt, we cannot generalize the results to the whole population of Egyptian TB patients.

In conclusion, the main factors associated with defaulting from the national programme of TB control in Alexandria, Egypt, were service-related factors, which are amenable to improvement. Expanding treatment outlets in rural settings, involving providers who practice close to where patients live, offering psychological support and health education programmes especially for younger patients, reduction of patient waiting times and improvement of patient–physician communication are recommended improvement strategies.

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