Implementation of Directly Observed Short Course Therapy for Tuberculosis

¹G.R. Irajian, ²M. Nassaji, ³R. Ranjbar, ⁴A. Beheshti, ⁵R. Ghorbani, ¹S. Salmanzadeh-Ahrabi, ²S. Ramazanzadeh, ⁶E. Moshiri, ³A. Karami, ³M.J. Hosseini, ⁷N. Bazzaz, ⁷N. Jonaidi Jafari and ⁷M. Izadi ¹Department of Microbiology, Semnan University of Medical Science, Semnan, Iran ²Fatemieh Hospital, 17 Shahrivar Blvd, Semnan, Iran ³Molecular Biology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran ⁴Faculty of Nursery, Semnan University of Medical Science, Semnan, Iran ⁵Semnan University of Medical Science, Semnan, Iran

⁶Department of Diseases Control and Prevention, Semnan University of Medical Science, Semnan, Iran ⁷Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Abstract: In this study, directly observed short course therapy (DOTS) was implemented to control tuberculosis in a camp in Iran. First, one study had been conducted in 1996 (before DOTS implementation) as active case finding then DOTS have been implemented in 1997. Another study was carried out in 2004 for evaluation of the effects of DOTS. In the first study, 16 patients with pulmonary TB (50% smear positive) were detected. During the years of DOTS implementation, the number of TB cases decreased significantly. In the second study, no pulmonary TB was detected. Our experience showed that DOTS significantly and effectively decreases TB in refugees and leads to a high cure rate and prevents death.

Key words: DOTS, refugees, tuberculosis

INTRODUCTION

Worldwide, tuberculosis (TB) is the leading cause of death (2-3 million deaths per year). TB has a devastating impact especially on developing nations. Crowding, poverty, war and immigration are impeding factors for control of TB (Fitzgerald and Haas, 2005).

Review of literatures show that immigrants and refugees in different parts of the world suffer from high rate of various diseases especially TB due to their living styles, health and nutritional conditions and crowding and poverty. They are more likely to have active and latent TB (Smith et al., 2000; Rysstad and Gallefoss, 2003; Hadzibegovic et al., 2005). Experiences show that despite of the difficult field conditions; control programs can be managed successfully in this setting and will reduce morbidity, mortality and transmission rates among refugees (Bodiang, 2000).

In 1993, WHO declared TB as a global health emergency and introduced directly observed therapy short course (DOTS) as the global TB control strategy. By implementing DOTS, WHO believed that TB prevalence and death could be reduced (Brewer and Heymann, 2004).

DOTS have five elements including political commitment, diagnosis by sputum smears, short course treatment with direct observation, regular drug supply and systematic monitoring. The international targets for TB control are to detect 70% of new pulmonary smear positive cases and to treat 85% of them successfully (Frieden *et al.*, 2003).

In Afghanistan, long lasting wars caused that effective TB treatment and control have not been implemented. Mortality and morbidity due to TB remained alarmingly high. Current estimates show that the incidence of active TB is 278/100000 (Khan and Laaser, 2002).

Even before US war, Afghans' health status was critically poor. They suffer from diseases associated with poor nutrition and sanitation. Increasing number of TB among Afghan refugees have been observed. Overcrowding and lack of sanitation and treatment facilities increase the risk of transmission in refugee camps (Shargie and Lindtjorn, 2005).

Within a decade from the war in Afghanistan, arrival of about 3 million Afghan refugees had a major effect on the epidemiology of TB in Iran. The annual burden of TB

was significantly higher than that reported by Iran ministry of health for entire population. So health authorities have taken an active approach for controlling of infectious diseases especially TB in refugees.

Iran's government established many camps for Afghan refugees. One of these camps was based in Semnan province in 1985 that settled about 3000 refugees. In 1997 health and medical education ministry of Iran introduced DOTS strategy to the entire of the country. The program rapidly expanded and covered all population. All provinces prepared a plan for implementation of the project based on detailed guidelines of WHO and assistance from the ministry of health.

Each district hired full-time trained physician as TB-Control officer and trained treatment and Laboratory supervisors, also provided microscopic centers and drug supplies. In most regions, community volunteers have given directed observed therapy supervised by local health office.

Each month every TB unit submits standardized reports on case detections, treatment outcomes and progress logistics to the province's TB unite and from there to ministry. All health care services and supplies were provided free to the whole populations.

By the beginning of DOTS in Iran this project also implemented in a refugee camp in Semnan. All elements were free for them. Three volunteers among refugees were trained for observation of DOTS, especially of treatment. A trained general physician attended in health station in camps twice weekly. All suspected to TB patients were referred to district TB center.

To determine the efficacy of DOTS on control of TB among the residents of this camp, two studies were carried out for comparing prevalence of TB before and after implementation of DOTS through 8 years.

MATERIALS AND METHODS

In 1996 (before implementation of DOTS) a study was carried out as active case finding in the camp of Afghan refugees in Semnan, Iran. All 15 years old and older camp residents were enrolled. A general physician, one healthcare worker and three refugees were voluntarily educated for becoming familiar with the study plan.

Refugees who transiently stayed in the camp were excluded and approximately 897 were included according to study inclusion criteria. For all person demographic data (age, gender) and history of BCG vaccination and family history of TB enlisted.

After teaching for proper expectoration (although trivial), three sputum samples were collected in covered

container from each person. They were also visited by physician for clinical signs of pulmonary TB (cough, hemoptysis, fever, anorexia, obvious weight loss and night sweating). Those with the presence of clinical signs and negative smears or only one positive smear underwent chest radiography. According to the smear examination, clinical symptoms and chest x-ray features and based on WHO guidelines they were classified as:

- **Smear positive pulmonary TB:** Those with at least 2 positive smears or one positive smear plus positive x-ray and clinical findings.
- Smear negative pulmonary TB: Those with 3 negative smears and positive x-ray and clinical findings.

All TB patients were treated with short course therapy and their family were screened for undiagnosed TB.

After this study, in 1997 all elements of DOTS project were implemented in the camp along with passive case finding and active screening of household contact of pulmonary TB patients.

Policy direction and supervision of drugs, treatment and Laboratory equipments were provided by the central health office. Supervision of the general health service staff in the camp was emphasized. The quality of the program maintained under regular supervision.

Another study took place in 2004 (8 year after DOTS implementation) for active detection of TB patients. In this study all refugees who were 15 or more years old (1397 persons) were evaluated for clinical symptoms of pulmonary TB. Eighty persons had cough and/or hemoptysis. No other symptoms of TB were detected. Two of these cases were excluded due to returning to Afghanistan. Three sputum smears, a sputum culture for mycobacterium tuberculosis and a chest x ray were done for all symptomatic cases. Other data enlisted were age, gender, past and family history of TB. Data were analyzed with SPSS software version 10.

RESULTS AND DISCUSSION

During the first study in 1997, 16 patients with pulmonary TB consisting of 8 smear positive (50%) and 8 smear negative (50%) TB were detected. Of these 3 patients (17.8%) were male and 13 (81.2%) were female. Table 1 shows prevalence of clinical findings in TB patients. Three patients had history of BCG vaccination (with visible scar) and 3 had family history of pulmonary TB.

Table 1: Clinical findings of disease among the pulmonary TB patients (1996)

Symptoms	N (%)
Cough	10 (62.5)
Hemoptysis	4 (25.0)
Fever	12 (75.0)
Anorexia and weight loss	12 (75.0)
Night sweating	11 (68.8)

Table 2: Reported TB cases in the refugee camp

Years	SPT*	SNT^{\dagger}	\mathbf{P}^{\ddagger}	EPT⁵	Comment
1995	-	3	111.0	-	
1996	9	7	592.5	1	First study
1997	1	7	296.0	-	DOTS
1998	2	2	148.0	-	
1999	2	-	74.0	-	
2000	-	-	0.0	-	
2001	3	-	111.0	-	
2002	-	1	37.0	-	
2003	-	-	0.0	-	
2004	-	-	0.0	-	Second study

^{*:} Smear positive pulmonary TB; †: Negative; ‡: Prevalence/100,000; §: Extra pulmonary TB

Table 3: Clinical findings of the disease among the cases in 2004 study

Symptoms	N (%)
Cough	61 (78.2)
Hmoptysis	6 (7.7)
Cough+Hemoptysis	11 (14.1)
Total	78 (100.0)

During 8 years of implementation of DOTS strategy, there was a dramatic decrease in TB among refugees (Table 2). There was no new smear positive TB from 2002. Treatment outcomes were excellent. There was no death, treatment failure or drug resistance during within 8 years period.

During the study in 2004, 1397 refugees (50.75% female and 49.25% male) were evaluated for clinical signs of TB. Of 78 patients who were suspected (Table 3), all were smear, culture and x-ray negative. Age distribution of these patients was between 16 and 90 years old, 22 had been treated for TB previously and 18 had positive family history for TB.

Tuberculosis is a preventable and curable disease in almost any socioeconomic circumstances especially with implementation of DOTS. Although TB controlling is a government job, it cannot be accomplished by any one individual or sector. It requires communications and collaborations among local and national health authorities and systems, hospitals, medical schools, private physicians, non-governmental organizations and others. Analysis of cost effectiveness suggests that treatment of TB with DOTS is as cost effective as ORS or measles vaccination (Marrero et al., 2001).

There are some lessons from present study that support above opinions: first, present study showed that TB prevalence was very high among refugees before implementation of DOTS, mainly because they were from

a country with high TB prevalence. Our study showed TB prevalence of 592.6/100,000 in 1996. It is very high especially when compared with TB burden among native Iranians in the same time (25.1/100000). In a study on refugees from Kosovo, there was a high rate of TB. Second, active case finding can be very effective especially in high rate groups and in limited populations. Active screening for TB has been done in industrialized countries, but with improvement in diagnosis and treatment it has been abandoned in most countries with low or medium TB incidence. It is still used in some countries with high rates of TB particularly in Eastern Europe and in selected populations (Monney and Zellweger, 2005). In 1995 the prevalence of TB diagnosed in the camp was 111/100000. In 1996 by active case finding it reached to 592.6/100000 that is very significant. Active screening also allows the detection of TB in earlier stages. It is possible that the yield of active case finding is higher among immigrant groups with very high incidence rates of TB. Third, DOTS project is a practical implemental strategy even in populations with poor conditions like refugees. In Iran, the plan covered most refugees. In china within less than 5 years, DOTS converge expanded from zero to more than 90% of target population (Xianyi et al., 2002).

Fourth, this study showed that DOTS is very effective in controlling of TB. In this camp TB prevalence fell down from 592.6/100000 to near zero after 5 years of DOTS and there wasn't new pulmonary TB since 2002. Many other studies support effectiveness of DOTS. In TB control project area in china the prevalence of disease fell by about 30% after 7 years of DOTS compared with non-project area (CTCC, 2004). In Peru, 10 years of intensive control caused decrease in national rate of TB (5.8% or more per year) (Suarez et al., 2001).

In Cuba with application of close supervision, systematic evaluation and DOTS strategy there was an annual decrease in new cases of 5% per year from 1965 to 1991 and 9.6% from 1991-96 (Marrero *et al.*, 2001). In New York there was 21% decrease in TB cases even in high risk groups from 1992 to 94 (Frieden *et al.*, 1995).

In Thailand, improving TB control caused 45% reduction during 20 years (Sawert *et al.*, 1997) and in Catalonia 30% reduction occurred between 1992 and 1997 (Alcaide *et al.*, 1999).

Fifth, DOTS effectively prevents death and treatment failure. During this period there was no case of death from TB among refugees, no treatment failure and no drug resistance. Other studies showed that DOTS reduced death and treatment failure (Shargie and Lindtjorn, 2005; Khatri and Frieden, 2002; CTCC, 1996).

Success in this setting was probably due to the tight controlling of refugees, highly motivated staffs and very good supports from health authorities. Successful global implementation of DOTS can save millions of lives. Applying control strategies advocated by WHO is a very good example of fighting against TB. It is also effective in refugees who usually have bad conditions from many aspects. The benefits of DOTS for individual patients and society are obvious.

If appropriate policies are followed and coordinated efforts are done within and outside of health sector, we can be ensured that TB can be controlled especially in limited and defined populations (asylums, villages, small towns, etc.). Active periodic case finding is also recommended in under controlled populations and areas with high burden of TB.

REFERENCES

- Alcaide Megias, J., J. Pascual Torramade, M.N. Altet Gomez, J. Maldonado Diaz de Losada, F. Lopez Espinosa and L. Salleras Sanmarti, 1999. Results and epidemiological impact of directly observed treatment of tuberculosis. Arch. Bronconeumol., 35: 267-274.
- Bodiang, C.K., 2000. Issues facing TB control. Tuberculosis control in refugee populations: A focus on developing countries. Scott. Med. J., 45: 25-28.
- Brewer, T.F. and S.J. Heymann, 2004. To control and beyond: MOVING towards eliminating the global tuberculosis threat. J. Epidemiol. Commun. Health, 58: 822-825.
- CTCC (China Tuberculosis Control Collaboration), 1996.
 Results of directly observed short-course chemotherapy in Chinese patients with smear-positive tuberculosis. Lancet, 347: 358-362.
- CTCC (China Tuberculosis Control Collaboration), 2004. The effect of tuberculosis control in China. Lancet, 364: 417-422.
- Fitzgerald, D. and D. Haas, 2005. *Mycobacterium tuberculosis*. In: Principles and Practice of Infectious Diseases. Mandell, G.L., J.E. Bennett and R. Dolin (Eds.), Philadelphia: Elsevier Churchill Livingstone, pp: 2855-2859.

- Frieden, T.R., P.I. Fujiwara, R.M. Washko and M.A. Hamburg, 1995. Tuberculosis in New York Cityturning the tide. N. Engl. J. Med., 333: 229-233.
- Frieden, T.R., T.R. Sterling, S.S. Munsiff, C.J. Watt and C. Dye, 2003. Tuberculosis. Lancet, 362: 887-899.
- Hadzibegovic, D.S., S.A. Maloney, S.T. Cookson and A. Oladele, 2005. Determining TB rates and TB case burden for refugees. Int. J. Tuberc. Lung. Dis., 9: 409-414.
- Khan, I.M. and U. Laaser, 2002. Burden of tuberculosis in Afghanistan: Update on a war-stricken country. Croat. Med. J., 43: 245-247.
- Khatri, G.R. and T.R. Frieden, 2002. Controlling tuberculosis in India. N. Engl. J. Med., 347: 1420-1425.
- Marrero, A., J.A. Caminero, R. Rodriguez and N.E. Billo, 2001. Towards elimination of tuberculosis in a low income country: The experience of Cuba, 1962-97. Thorax, 56: 84-85.
- Monney, M. and J.P. Zellweger, 2005. Active and passive screening for tuberculosis in Vaud Canton, Switzerland. Swiss. Med. Weekly, 135: 469-474.
- Rysstad, O.G. and F. Gallefoss, 2003. TB status among Kosovar refugees. Int. J. Tuberc. Lung Dis., 7: 458-463.
- Sawert, H., S. Kongsin, V. Payanandana, P. Akarasewi, P.P. Nunn and M.C. Raviglione, 1997. Costs and benefits of improving tuberculosis control: The case of Thailand. Soc. Sci. Med., 44: 1805-1816.
- Shargie, E.B. and B. Lindtjorn, 2005. DOTS improves treatment outcomes and service coverage for tuberculosis in South Ethiopia: A retrospective trend analysis. BMC. Public Health, 5: 62.
- Smith, A., D. O'Flanagan, D. Igoe, J. Cronin, D. Forde and E. McArdle *et al.*, 2000. Outcome of medical screening of Kosovan refugees in Ireland: 1999. Commun. Dis. Public Health, 3: 291-294.
- Suarez, P.G., C.J. Watt, E. Alarcon, J. Portocarrero, D. Zavala and R. Canales *et al.*, 2001. The dynamics of tuberculosis in response to 10 years of intensive control effort in Peru. J. Infect. Dis., 184: 473-478.
- Xianyi, C., Z. Fengzeng, D. Hongjin, W. Liya, W. Lixia and D. Xin et al., 2002. The DOTS strategy in China: Results and lessons after 10 years. Bull. WHO., 80: 430-436.