FACTORS CONTRIBUTING TO POOR COMPLIANCE WITH ANTI-TB TREATMENT AMONG TUBERCULOSIS PATIENTS

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Abstract. Tuberculosis (TB) has made a comeback. It has become a resurgent public health problem in developing countries in the tropics and is the leading cause of death from any single infectious agent. Non-compliance to anti-tuberculosis treatment is the most serious problem in TB control. A cross-sectional study was conducted to investigate the determinants of poor compliance with anti-tuberculosis treatment among tuberculosis patients in Kota Bharu, Kelantan, Malaysia in 1999. A total of 390 patients were included in the study of which 130 were tuberculosis patients who defaulted treatment and 260 were those compliant to treatment. Data collection was done by interviewing the patients and collecting clinical and laboratory data from their medical records. Using multiple logistic regression analysis, patients who were not on direct observed therapy (DOT) lived distant to the health facility, were non-intravenous drug users (IVDU) and were HIV positive had statistically significant higher odds of being non-compliant. Patients should be given treatment under direct supervision with special attention to IVDU and HIV positive groups. Anti-TB treatment should be accessible to patients at the nearest health center from their residence. Interventions with health education programs emphasizing the benefits of treatment compliance should be implemented by further large-scale multi-centered studies.

INTRODUCTION

Tuberculosis (TB) has been declared a global public health emergence by the World Health Organization (WHO) (Kochi, 1991; WHO, 1992). The disease causes significant mortality and morbidity globally and with the advent of the human immune deficiency virus (HIV) epidemic, TB is regarded as a worldwide public health challenge (Kochi, 1991; WHO, 1992). The rising incidence of TB due to the effect of HIV in both developed and developing countries is well recognized (Narain *et al*, 1992).

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The highest prevalence and estimated annual risk of TB infection are in sub-Saharan Africa and Southeast Asia. TB is one of the most widespread diseases affecting 8-10 million new cases annually and nearly 3 million deaths occur worldwide each year. About one-third of the world population is latently infected with *Mycobacterium tuberculosis* with more than 95% of these in the developing world. TB kills more people than any other single infectious agent and death from TB comprises 26% of all avoidable deaths in developing countries (WHO, 1992).

Besides well-known risk factors, the most important unresolved challenge in TB control is the treatment completion. Treatment will only be effective if the patient completes the regimen which includes a combination of drugs recommended by the physicians. Poor compliance contributes to the worsening of the

TB situation by increasing incidence and initiating drug resistance. Resistance to anti-TB drugs has also emerged as an important obstacle in the control of the disease. World-wide patient compliance with anti-TB therapy, with an estimate of as low as 40% in developing countries, remains the principle cause of treatment failure (Fox, 1983). The critical aspect of management is ensuring compliance with a full course of chemotherapy (Cuneo and Snider, 1989). The World Health Organization recommends at least 85% cure rate of all diagnosed TB cases (WHO, 1992). In order to achieve this cure rate, compliance needs to be in the order of 85-90 % (Murray *et al*, 1990).

It is therefore beneficial to study factors related to poor compliance, default and abandonment of treatment, which are responsible for drug resistance and increased incidence of TB. Factors that have been reported as being associated with increased compliance by many studies were directly observed therapy (Feinstein *et al*, 1959; 1968; Jonson and Freeman, 1972; Stradling and Poole, 1970; Strong, 1970; Chaulet *et al*, 1967; Albert *et al*, 1976) and combined short-course regimen (WHO, 1991). On the other hand, factors that were found as being associated with poor compliance were HIV infection, poverty, increasing immigration (Barnes and Barrows, 1993; Drucker *et al*, 1994; Cantwell *et al*, 1994; Brudney and Dobkin; 1991), intravenous drug user status, alcoholics, unemployment (Brudney and Dobkin, 1991a,b; Ferrer *et al*, 1991; Crespo *et al*; 1992), poor belief and motivation and perceived susceptibility to disease (Rosenstock, 1975; Sloan and Sloan, 1981).

In Malaysia, the incidence of tuberculosis was 58 per 100,000 and mortality rate was 3.4 per 100,000 population in 1997 (Abdullah, 1996), which is still considered low compared to other developing countries in the region. In the state of Kelantan, with the decline in the incidence of other infectious diseases, TB has in turn become the leading infectious disease with the highest incidence rate in the state. The incidence rate for 1997 was 53.6 per 100,000 population, which is about that of the national average rate. The number of defaulters has also increased along with the higher incidence rate. In Kota-Bharu alone which is the capital of Kelantan State, the range of defaulters amongst TB patients were between 124-315 (20% to 43%) during the period of 1990 to 1997. Patients who abandoned treatment accounted for 2.5-5.2 % of TB patients for the same period (Anonymous, 1996-1999).

In this regard, a study was conducted to assess non-compliance and determine treatment-related factors, disease related factors, knowledge and attitude related factors and socio-demographic factors, which may have influenced the poor compliance of TB patients towards anti-TB treatment in Malaysia. Even though similar studies have been done in other parts of the world, there was still a need to conduct this study in this region as there are differences compared to other countries in many aspects such as culture, demography, socio-economic status, knowledge level, drugs used, tolerance to the side effects of drugs. The results of other studies may not be relevant to apply to the context of this region. The expected benefits from conducting this study included determining possible solutions to the existing treatment default problem, to help reduce the transmission and incidence of TB and to contribute towards the improvement of TB control programs especially in planning intervention measures.

MATERIALS AND METHODS

A cross-sectional study was conducted between January and December 1999 at the chest clinic, Kota Bharu General Hospital, Kelantan, Malaysia. The study population was TB patients registered at the state chest clinic, Kota Bharu General Hospital. All subjects were confirmed as TB patients by clinical examination and laboratory investigations (sputum for acid fast bacilli positive status, chest X-ray, Tuberculin test). Patients were referred by other health facilities if they were

suspected of suffering from TB and diagnosed and treated at the state chest clinic. Patients were ineligible for the study if they were too ill to be interviewed, were suffering from psychiatric illness and gave an incorrect address or could not be traced or died. There was no age exclusion.

The frequency and duration of usual treatment for each patient at the chest clinic is determined by the physician. There were different treatment regimens which consisted of a combination of two or three or four standard anti-TB drugs namely streptomycin, isoniazid, rifampicin and pyrazinamide. Frequency and duration were daily for two months or biweekly for four months or one year. Streptomycin was administered by parenteral route and the rest were by oral route. The dosages differed between adults and children.

If the patients did not turn up for treatment during the course, they were reminded at their residence by phone call or mail. If they still did not respond, chest clinic staff visited their residence and brought them back to the chest clinic for continuation of treatment (known as retrieval). This retrieval process was applied anytime during the course of treatment whenever the patient was not compliant to treatment. There was no particular follow-up during treatment unless the patient had complaints such as side effects of drugs. After the completion of the course of treatment there was a thorough follow-up medical check-up which consisted of physical examinations, chest X-ray and biochemical investigations. This follow-up was done as early as one month after the completion of treatment.

The definitions of compliance and non-compliance were determined by the Ministry of Health based on World Health Organization guidelines. Compliance was defined as completion of prescribed treatment or as missing less than 25% of treatment within the specified duration. Patients who complied with treatment but had not completed the treatment course, were also excluded from the study since their final compliance status was yet to be determined. The compliant patients were recruited to the study only when they came for follow-up one month after completion of the course of treatment. They were eligible to be included into study at the very first visit for follow-up for clinical check-up and other laboratory tests after treatment completion.

Non-compliance was defined as missing more than 25% of treatment in a month [*ie* missed more than one week injection (daily/intermittent) or missed more than one week for collection of oral drugs] (known as defaulters) or defaulting for more than one month (known as abandoned treatment). The non-compliance group also included patients who defaulted the treatment and were later retrieved through any means *ie* home visits, letter, returned of own accord, etc (known as defaulter retrieval) or patients who abandoned treatment but were retrieved by bringing back or returned of his or her own accord for resumption of treatment (known as abandoned treatment retrieval). Non-compliance was identified by a registry, which was regularly updated and medical records were also checked for confirmation of non-compliance.

The procedure for the recruitment of patients involved chest clinic staff who identified TB patients registered between the period of January and December 1999 as compliant and non-compliant according to definitions mentioned above. The sample excluded those whose compliance status could not be determined because treatment was not yet completed at the end of 1999 when the study period ended. The research team was present at the chest clinic on clinic days which were regularly conducted three days per week. When the compliers attended the clinic for follow-up or non-compliers were retrieved for treatment, the chest physician indicated whether the patient was eligible to be included in the study. The chest physician referred eligible patients for study to the researchers who were stationed next door to the examination room. Research staff approached eligible patients, explained the study and recruited those who agreed to participate in the study. Non-com-

pliant patients, who could not be retrieved after many attempts by reminder letters, were contacted by phone at their residence. Those who could not be traced, who died, who did not consent or who gave wrong address were excluded from the study. Home visits were made to those who consented and those who met the inclusion criteria. All patients were briefed during the interview and informed consent was taken before data collection. Data were collected by interviewing individual patients. A public health inspector from the chest clinic accompanied the research team as part of routine retrieval process.

Disease related factors were obtained by physician during history taking and physical examination sessions when patients were diagnosed as TB. The research team collected this information from medical records of patients. Two trained research assistants conducted the interviews and completed the questionnaires for both compliance and non-compliance groups (for non- compliance group, either at chest clinic or at their residence). The responses from the patients who were younger than 15 years old were counterchecked by asking their accompanying parents or guardians. The results of laboratory investigations and other information were also collected from the medical records of individual patients.

The questionnaire which had been pretested on 50 patients prior to data collection included the following variables: (1) socio-demographic and other related factors such as age, gender, ethnicity, marital status, educational level, occupation, family income, nationality, residential locality (urban/rural), (2) knowledge about TB and attitude towards anti-TB treatment, (3) treatment related factors such as treatment regimen, knowledge about complete dosage of treatment, mode of therapy, side effects of oral and parenteral drugs, problem with distance between residence and treatment center, waiting time, direct observed therapy (DOT) status, (4) disease related factors such as site of tuberculosis (pulmonary/extra-pulmonary), sputum smear result, severity of the disease, type of tuberculosis (first time diagnosis/relapse/multi-drug resistant tuberculosis) and human immuno-deficiency virus (HIV) carrier status, and (5) other risk factors such as BCG vaccination status, presence of BCG scar, smoking habit, alcohol intake, intravenous drug user (IVDU) status, movement of residence during the course of treatment and satisfaction with services and staff receptiveness towards patients. The questionnaire was constructed based on factors demonstrated previously to be related to non-compliance or considered to be clinically important.

Statistical analysis

Sample size calculation was based on the estimated proportion of compliance among TB patients, which was about 50%. The required sample size for estimation of proportion of compliance with 95% confidence interval within ±5% of point estimate was 384 TB patients. Sample size for determination of factors contributing to poor compliance was also calculated based on the variable of interest (exposure) non-DOT. DOT was about 60% in compliance group and 40% in non-compliance group. Power of the study was set at 80%. The ratio of non-compliance and compliance groups was 1:1. The required sample size was 107 patients for each group. Based on the required sample size and number of patients available according to previous years' statistics, it was decided that recruitment of all patients within given timeframe (January to December 1999) would provide adequate sample size.

Data entry was done by using Epi-Info version 6.04. Data analysis was done by using SPSS version 10.0. Subjects were classified as compliance and non-compliance based on criteria described above and were treated as dichotomous binary outcome. Some continuous variables (*eg* age) were transformed into categorical variables for better interpretation and understanding. Univariate analysis by using simple logistic regression and two-way tables was applied to predict the potential determinants. The criteria for selecting potential

variables to be included in multivariate analysis was based on statistically significant variables by univariate analysis ($p<0.25$) and variables proven by other studies to be significantly associated with poor compliance. Backward stepwise multiple logistic regression procedure was performed to determine factors associated with non-compliance adjusted for confounders. The final best model was obtained by considering the importance of statistical significance, biological plausibility, variables of clinical importance and variables proven as risk factors by previous studies. Maximum likelihood ratio estimation was used to estimate parameters and goodness of fit was applied to assess models. The likelihood ratio (LR) test was used to assess the statistical significance and a 5% significance level was used.

RESULTS

There were 709 TB patients who attended chest clinic during study period. A total of 309 patients completed anti-TB treatment. Among the other 400 patients, 237 were not compliant. A total of 58 patients could not be recruited as they had died and 105 were still undergoing treatment and were therefore ineligible for the study. Thus, the compliance rate was reported as 56.6% (309/546).

Among the compliant group, 299 patients were eligible for the study and when approached, 260 agreed to participate in the study. For 237 patients in non-compliance group, a total of 70 patients could be retrieved and among them, 51 were eligible for the study and when approached, 46 volunteered to be included in the study. Ineligibility of most of the patients in both groups was mainly because the patients were ill to be interviewed. Among 167 non-compliance patients who could not be retrieved, 26 patients gave wrong address and 50 patients could not be traced at home/ unwilling to accept home visit when contacted by phone. When home visits were made, seven patients were not at home or did not consent and 84 patients were willing to participate in the study. Therefore finally, there were 130 non-compliant and 260 compliant patients who were recruited to the study giving the ratio of non-compliance to compliance as 1:2. The response rates for compliance and non-compliance group were 87% and 60% respectively and it was statistically significantly different ($\chi^2=50.8$, $p<0.001$). It showed that non-compliant patients were more reluctant to participate in the study.

Among 390 patients recruited to the study, mean age was 43±17 years with a range of 6 to 84 years. A total of 66% of non-compliance group were males. The Malay ethnic group was predominant comprising 94% of all patients. Site of the disease was predominantly pulmonary (89%) cases. Majority of patients fell into the category of mild and moderate severity of disease by X-ray findings. Among 63 intravenous drug users, 11% were HIV positive (7 out of 63).

On univariate analysis, there were no significant differences in socio-demographic characteristics between non-compliance and compliance groups (Table 1). Among attitude variables, health seeking attitude towards treatment (over the counter treatment) was found of borderline significance which was marginally better in compliance group (Table 2). Among treatment related factors, there were significant differences between compliance and non-compliance groups regarding convenience with clinic day schedule (those who were inconvenient with schedule had about 2.5 times higher odds of being non-compliant), DOT (those who were not on DOT had seven times higher odds of being non-compliant), problem with distance to health facility (those who had problem with distance had two times higher odds of being non-compliant) and patients who lived more than ten kilometers away from health facility had seven and half times significantly higher odds of being non-compliant (Table 3). Disease related factors did not show any significant difference between two groups (Table 4). Among other contributing factors, intravenous drug

Table 1
Socio - demographic factors contributing to poor compliance with anti-TB treatment (Univariate analysis).

Variable			Non-compliance (n)(%)	Compliance (n)(%)	Odds ratio (95% CI)	[a]LR (p-value)
Sex	Male	248	86 (66)	162 (62)	1	0.56 (0.456)
	Female	142	44 (34)	98 (38)	1.18 (0.76-1.84)	
Age group	≤20	36	9 (7)	27 (10)	1	2.30 (0.890)
	21-40	160	57 (44)	103 (40)	1.34 (0.54-3.29)	
	41-60	118	38 (29)	80 (31)	0.56 (0.21-1.51)	
	>60	76	26 (20)	50 (19)	0.86 (0.31-2.37)	
Residence						
Urban		151	51 (39)	100 (38)	1	0.02 (0.883)
Rural		239	79 (61)	160 (62)	0.97 (0.63-1.49)	
Marital status						
Married		268	93 (72)	175 (67)	1	0.82 (0.664)
Never married		88	26 (20)	62 (24)	0.79 (0.47-1.33)	
Widow / Divorce		34	11 (8)	23 (9)	0.90 (0.42-1.93)	
Ethnic group						
Malay		367	122 (94)	245 (94)	1	0.02 (0.880)
Chinese and Siamese		23	8 (6)	15 (6)	1.07 (0.44-2.60)	
Level of Education						
Tertiary and Secondary		213	70 (54)	143 (55)	1	0.16 (0.923)
Primary		118	41 (31)	77 (30)	1.08 (0.68-1.75)	
Uneducated/not yet schooling		59	19 (15)	40 (15)	0.97 (0.53-1.80)	
Occupation						
Government Servant		41	12 (9)	29 (11)	1	12.28 (0.139)
Own business		25	9 (7)	16 (6)	1.46 (0.39-5.39)	
Labourer+farmer		27	6 (5)	21 (8)	1.33 (0.36-4.87)	
Housewife		83	30 (23)	53 (20)	1.62 (0.59-4.44)	
Unemployed		68	28 (21)	40 (15)	2.43 (0.88-6.68)	
Student		32	4 (3)	28 (11)	1.08 (0.30-3.92)	
Retired		25	10 (8)	15 (6)	0.51 (0.09-2.73)	
Others		89	31 (24)	58 (23)	0.91 (0.32-2.62)	
Monthly average income						
Low (< RM 1,000)		354	119 (92)	235 (90)	1	0.14 (0.709)
Middle and high (≥RM 1,000)		36	11 (8)	25 (10)	0.87 (0.41-1.83)	

[a]Likelihood ratio test statistic and corresponding p-value.

user status was found significant between two groups. Patients who were not intravenous drug users had about 2.5 times higher odds of being non-compliant (Table 5). Crude odds ratio with its corresponding 95% confidence intervals, Likelihood Ratio statistic and its corresponding p-values were shown in univariate tables.

On multivariate analysis, variables that were found as significant predictors were DOT, distance between residence and health facility, intravenous drug user status and HIV status of the patients. Patients who were not on DOT had three times, patients who lived more than ten kilometers away from health facility had six times, patients who were not intravenous drug users had four times and patients who were HIV positive had three times statistically significant higher odds of being non-compliant (Table 6). Adjusted odds ratio with its corresponding 95% confidence

Table 2
Knowledge and attitude factors contributing to poor compliance with anti-TB treatment (Univariate analysis).

Variable		Non-compliance (n)(%)	Compliance (n)(%)	Odds ratio (95% CI)	[a]LR (p-value)
Causes of TB					
Correct	215	74 (57)	141 (55)	1	0.95 (0.621)
Incorrect	43	16 (12)	27 (10)	1.13 (0.57-2.23)	
Do not know	132	40 (31)	92 (35)	0.83 (0.52-1.32)	
Spread of TB					
Correct	296	102 (79)	194 (75)	1	1.05 (0.592)
Incorrect	13	3 (2)	10 (4)	0.57 (0.15-2.12)	
Do not know	81	25 (19)	56 (21)	0.85 (0.50-1.44)	
Prevention of TB					
Correct	210	76 (68)	134 (57)	1	4.78 (0.092)
Incorrect	45	13 (12)	32 (13)	0.72 (0.35-1.45)	
Do not know	92	22 (20)	70 (30)	0.55 (0.32-0.97)	
Seriousness of TB					
Yes	328	115 (89)	213 (82)	1	3.95 (0.139)
No	36	7 (5)	29 (11)	1.22 (0.51-2.88)	
Do not know	26	8 (6)	18 (7)	0.54 (0.17-1.75)	
Preventable					
Yes	367	121 (93)	246 (95)	-	1.42 (0.493)
No	5	1 (1)	4 (1)	0.51 (0.06-4.06)	
Do not know	18	8 (6)	10 (4)	1.63 (0.63-4.23)	
Curable					
Yes	358	121 (93)	237 (91)	1	1.38 (0.503)
No	7	1 (1)	6 (2)	0.33 (0.04-2.74)	
Do not know	25	8 (6)	17 (7)	0.92 (0.39-2.20)	
Seeking treatment					
Hospital	318	109 (84)	209 (80)	1	7.63 (0.054)
General practitioner	38	16 (12)	22 (8)	1.39 (0.70-2.77)	
Traditional 5	1	(1) 4	(2) 0.48	(0.05-4.34)	
Over counter	29	4 (3)	25 (10)	0.31 (0.10-0.90)	

[a]Likelihood ratio test statistic and corresponding p-value.

intervals, Likelihood ratio statistic and its corresponding p-values were shown in multivariate results.

DISCUSSION

Compliance rate reported by this study was about the same as those found in some other studies (Nuwaha, 1997; Chuah, 1991). Completion of treatment rates were very low in many parts of the world such as in Bangladesh where only about 25% of patients completed treatment, although this improved to 60% with the use of an incentive scheme and village based health workers (Chowdhury *et al*, 1992).

In this study, patients who were not on DOT had three times significantly higher odds of being non-compliant. This finding strongly supported other studies conducted throughout the world. Majority of compliant patients in this study were under DOT with parenteral therapy. Those under parenteral therapy were less likely to be non-compliant as they needed to visit health centers for treatment. A number of studies confirm good long - term compliance of patients when parenteral treatment is

Table 3
Treatment related factors contributing to poor compliance with anti-TB treatment (Univariate analysis).

Variable		Non-compliance (n)(%)	Compliance (n)(%)	Odds ratio (95% CI)	[a]LR (p-value)
Complete dosage					
Knows	373	127 (98)	246 (95)	1	2.19 (0.139)
Does not know	17	3 (2)	14 (5)	0.42 (0.12-1.47)	
Clinic days					
Convenient	128	60 (46)	68 (26)	1	15.39 (<0.001)
Inconvenient	262	70 (54)	192 (74)	2.42 (1.56-3.77)	
Regimen					
Long	51	12 (9)	39 (15)	1	2.67 (0.102)
Short	339	118 (91)	221 (85)	1.74 (0.88-3.44)	
Mode of therapy					
Oral only	73	23 (18)	50 (19)	1	0.14 (0.712)
Oral + parenteral	317	107 (82)	210 (81)	1.11 (0.64-1.92)	
DOT Yes	339	93 (72)	246 (95)	1	38.20 (<0.001)
No	51	37 (28)	14 (5)	6.99 (3.61-13.52)	
Side effects (oral)					
No	181	57 (44)	124 (48)	1	1.17 (0.556)
Mild / Moderate	22	6 (5)	16 (6)	0.82 (0.30-2.19)	
Severe	187	67 (51)	120 (46)	1.22 (0.79-1.87)	
Side effects (parenteral)					
No	114	39 (31)	75 (30)	1	0.68 (0.711)
Mild / Moderate	20	5 (4)	15 (6)	0.70 (0.29-1.72)	
Severe	256	83 (65)	163 (64)	0.98 (0.61-1.57)	
Problem with distance					
No	337	104 (80)	233 (90)	1	6.51 (0.011)
Yes	53	26 (20)	27 (10)	2.16 (1.20-3.88)	
Distance to health facility					
≤10 km	317	78 (60)	239 (92)	1	55.13 (<0.001)
>10 km	73	52 (40)	21 (8)	7.59 (4.30-13.38)	
Waiting time					
Short	292	98 (75)	194 (75)	1	0.03 (0.869)
Long	98	32 (25)	66 (25)	0.96 (0.59-1.56)	

[a]Likelihood ratio test statistic and corresponding p-value.

used (Feinstein *et al*, 1959; 1968; Jonson and Freeman, 1972; Stradling and Poole, 1970; Strong, 1970; Chaulet *et al*, 1967; Albert *et al*, 1976). Directly observed therapy, in particular, has proven effective against the resurgence of TB and the emergence of drug resistance and is cost - effective (Iseman *et al*, 1993; Weis *et al*, 1994; Chaulk *et al*, 1995). The success of DOT has led some authors and organizations in the United States to call for universal DOT or at least to consider it in every patient (Iseman *et al*, 1993; Dubler, 1992). The high risk of treatment default, the difficulties in predicting adherence, and the serious public health consequences of non-adherence documented in many studies lend strong support to the use of DOT. Until better strategies are developed, DOT should be offered to every patient, with appropriate individualized enablers and creative delivery schemes (Pablos *et al*, 1997).

In this study as well as in the study conducted in Northwest Perak of Malaysia

Table 4
Disease related factors contributing to poor compliance with anti-TB treatment (Univariate analysis).

Variable		Non-compliance (n)(%)	Compliance (n)(%)	Odds ratio (95% CI)	[a]LR (p-value)
Sputum smear					
Positive	379	128 (98)	251 (97)	1	1.30 (0.255)
Negative	11	2 (2)	9 (3)	0.44 (0.09-2.05)	
Site					
Pulmonary	348	118 (91)	230 (88)	1	0.49 (0.483)
Extra-pulmonary	42	12 (9)	30 (12)	0.78 (0.39-1.58)	
Severity (by x-ray)					
Mild	221	71 (54)	150 (58)	1	3.37 (0.186)
Moderate	128	40 (31)	88 (34)	0.96 (0.60-1.53)	
Severe	41	19 (15)	22 (8)	1.83 (0.93-3.59)	
Diagnosis					
First time diagnosed	353	118 (91)	235 (90)	1	0.02 (0.903)
Relapse	37	12 (9)	25 (10)	0.96 (0.47-1.97)	
HIV status					
Negative	272	122 (94)	250 (96)	1	1.01 (0.316)
Positive	18	8 (6)	10 (4)	1.64 (0.63-4.26)	

* Likelihood ratio test statistic and corresponding p-value

Table 5
Other factors contributing to poor compliance with anti-TB treatment (Univariate analysis).

Variable		Non-compliance (n)(%)	Compliance (n)(%)	Odds ratio (95% CI)	[a]LR (p-value)
BCG vaccination status					
Yes	285	97 (75)	188 (72)	1	0.24 (0.627)
No	105	33 (25)	72 (28)	0.89 (0.55-1.44)	
BCG scar					
Yes	283	97 (75)	186 (72)	1	0.42 (0.519)
No	107	33 (25)	74 (28)	0.85 (0.52-1.37)	
Smoking status					
Yes	184	66 (51)	118 (45)	1.24 (0.81-1.89)	1.01 (0.315)
No	206	64 (49)	142 (55)	1	
Alcohol taking					
Yes	16	7 (5)	9 (4)	1.59 (0.58-4.36)	0.78 (0.376)
No	374	123 (95)	251 (96)	1	
Intravenous drug user status					
Yes	63	12 (9)	51 (20)	1	7.47 (0.006)
No	327	118 (91)	209 (80)	2.40 (1.23-4.68)	
Change of residence					
Yes	37	12 (9)	25 (10)	1	0.02 (0.903)
No	353	118 (91)	235 (90)	1.05 (0.51-2.16)	
Satisfaction with staff					
Yes	383	126 (97)	257 (99)	1	1.69 (0.193)
No	7	4 (3)	3 (1)	2.72 (0.60-12.34)	

[a]Likelihood ratio test statistic and corresponding p-value.

Table 6
Significant factors contributing to poor compliance of anti-TB treatment (Multiple logistic regression analysis).

Variable	Odds ratio[a] (95% CI)	[b]LR (p-value)
DOT		
Yes	1	-
No	3.14 (1.45-6.81)	8.49 (0.004)
Distance between residence and health facility		
≤10 km	1	-
>10 km	6.00 (3.07-11.71)	29.02 (<0.001)
Intravenous drug user status		
Yes	1	-
No	4.11 (1.84-9.21)	14.25 (<0.001)
Human immuno-deficiency virus		
Negative	1	-
Positive	3.12 (1.08-9.02)	4.20 (0.040)

[a]Adjusted for other variables in multivariate analysis model.
[b]Likelihood ratio test statistic and corresponding p-value.

(Chuah, 1991), age and ethnic origin did not affect compliance. This was interesting since different religious beliefs and attitude of older and younger generations differ. In contrast in rural Pakistan (Sloan and Sloan; 1981), in-bred fears and supernatural beliefs were two major factors affecting patients' compliance with treatment. This study reported that there were no significant differences between non-compliance and compliance groups in terms of socio-demographic and other related factors such as family income and residential locality, treatment related factors such as knowledge about complete dosage of treatment, mode of therapy, side effects of oral and parenteral drugs, waiting time, disease related factors such as site of TB, sputum smear result, severity of the disease, type of TB, other factors such as satisfaction with services and staff receptiveness towards patients, BCG vaccination status, presence of BCG scar, smoking habit and alcohol intake. In compiling and indexing the world's literature on adherence, Haynes *et al* (1979) found that factors consistently associated with poor adherence included disabling psychiatric illnesses, long intervals between time of reference and appointment date, long treatment duration, complex medical regimens, costs associated with treatment, and medication errors (Haynes *et al*, 1979). On the other hand, age, gender, income, occupational status, and education were not consistent predictors of non-adherence (Haynes *et al*, 1979; Stephenson *et al*, 1993). The magnitude of the problem of non-compliance in tuberculosis depends on the definition used, the patient population, and the nature of local control programs (Brundney and Dobkin, 1991a,b; Moulding, 1966).

Many non-compliant patients expressed that distance between their residence and health facility was a problem. From this study, patients who lived more than ten kilometers away from health facility had six times significantly higher odds of being non-compliant. This finding however is in contrast with the results of another study conducted in the state of Perak, Malaysia where the distance from Taiping district general hospital and place of residence had no significant effect on defaulting behavior (Chuah, 1991).

This study showed that HIV positive patients had three times significantly higher odds of being non-compliant. The main rea-

son for this was parenteral therapy was contraindicated in HIV positive patients according to the protocol instructed by Ministry of Health and hence they were not on DOT. Therefore, adherence to treatment was more unlikely and they tend to become non-compliant. This finding is similar to the findings reported in many other studies. It is reported that the resurgence of TB has been attributed to the HIV infection, worsening poverty, increasing immigration, dismantling of control programs, and poor adherence to treatment (Barnes and Barrows, 1993; Drucker *et al*, 1994; Cantwell *et al*, 1994; Brudney and Dobkin; 1991a,b). The issues and recommendation on ways to implement programs that provide better anti-TB treatment to HIV positive patients should be considered seriously since higher mortality due to TB in HIV positive patients is well-documented. Every HIV positive patient should be administered drugs under the direct supervision of health authorities. Health education programs emphasizing association between TB and HIV would be highly beneficial.

Intravenous drug users tend to be more compliant to treatment as documented in this study. Compliance was significantly better among intravenous drug users compared to those who were not. Those patients who were not drug users had about four times higher odds of being non-compliant. The reasons being majority (86 %) of users were on DOT, special attention and advice to comply with treatment given by chest clinic staff, having strong family support and close observation for treatment was given when they were in prison or drug rehabilitation centers. This finding is in contrast to other studies. Several studies have documented increased rate of non-compliance among the homeless alcoholics, injection drug users, and unemployed patients (Brudney and Dobkin, 1991a,b; Ferrer *et al*, 1991; Crespo *et al*, 1992). Therapeutic compliance is a task-specific behavior amenable to interventions such as health education and treatment supervision.

Knowledge of factors associated with poor compliance can help identify groups at risk of defaulting and lead to improved patient's education. However, knowledge and attitude factors were not significant in this study. Other studies reported that patient's compliance with therapy is affected by issues of belief, health motivation, perceived susceptibility to disease and its severity, views in the benefit of professional intervention and knowledge of the condition (Rosenstock, 1975; Sloan and Sloan, 1981). These factors can be modified by improving the patient-doctor relationship and through health education (Francis *et al*, 1969).

With regard to health seeking attitude, it was interesting to note in this study that patients who were more in favor of over the counter treatment were less likely to become non-compliant. Health concern and cautiousness of these patients probably lead to their greater compliance to treatment. However, this health seeking attitude was borderline significant in univariate analysis and did not reach statistical significance by multivariate analysis in this study. If a patient is found to have tuberculosis, the responsible clinician has a legal obligation to refer him or her to the chest clinic. It means the patient is not the party taking the initiative. However, other forms of referral involve the patient taking the initiative to consult his or her family doctor, the local health center or directly visiting the chest clinic (Chuah, 1991).

There was no significant difference between non-compliers and compliers regarding the treatment regimen in this study. Most of the patients were under short-term therapy. The use of short course chemotherapy in improving compliance is well known (Murray *et al*, 1990). Short- course anti-TB regimens with isoniazid, rifampicin and pyrazinamide, with or without streptomycin or ethambutol as a fourth, have been recommended and used in all developed and some developing countries for treatment of pulmonary and extrapulmonary TB as their efficacy under controlled clinical trial conditions or program conditions have been well documented. Short - course regimens are now recommended by the World Health Organization (WHO), The International Union Against Tuberculosis and

Lung Disease (IUATLD), The British Thoracic Association and the American Thoracic Society (ATS) for treatment of TB in both developed and developing countries.

During data collection in this study, there were two different methods used. One was by interviewing the patients to collect information and the other was by collecting other variables from their medical records. It was inappropriate to obtain clinical data when the patient was undergoing a physical examination by the physician. In addition, variables needed for clinical data and results of laboratory investigations were clearly stated in medical records. Therefore, there was no room for bias during data collection since the nature of information obtained was different.

Logistic problems faced by this study were relatively few retrieval cases, poor cooperation from some patients, repeated home visits for retrieval cases and, deaths of HIV positive patients who had turned into full-blown AIDS cases during data collection. Practically and from an ethical point of view, only patients who were not very ill, mentally sound and willing to participate were included in the study only after being examined by medical doctors. The other point was that it was not easy to include non-compliant patients into the study since non-compliant patients were more reluctant to participate as reported in results. Finally, the other limitation of this study was that the compliance of patients was determined by chest clinic authorities according to the definitions of compliance and non-compliance set by the Ministry of Health. The determination of compliance did not include more specific methods such as biochemical test of urine or blood and pill counts at their residences. This is the weak part of this study.

Protracted tuberculosis among non-adherent patients contributed to the well-documented emergence and the spread of drug-resistant tuberculosis (Frieden *et al*, 1993; Bifani *et al*, 1996). Community-based TB treatment under direct observed therapy is until now the only effective way to reduce transmission and development of drug resistant tuberculosis. With the epidemic of HIV infection, special emphasis should be made with regard to TB patients who are HIV positive and who are intravenous drug users. Having identified patients who are likely to default, health education could then be efficiently directed to maximize patient's compliance (Chuah, 1991). New approaches are needed to combat the global tuberculosis epidemic (Wilkinson, 1994). It is hoped that results of this study will be utilized to improve planning and implementation of TB treatment by overcoming the problems regarding treatment completion. Future research should be focused on intervention programs to improve the knowledge and awareness of TB patients about the disease and its complications.

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