Assessment of Patient Adherence to Tuberculosis Treatment in Dessie Referral Hospital, South Wollo, Ethiopia

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ABSTRACT

Background: Poor adherence to treatment of tuberculosis is common despite various interventions aimed at improving treatment completion. Lack of a comprehensive and holistic understanding of barriers to and facilitators of, treatment adherence is currently a major obstacle to find effective solutions.
Objective: The purpose of this study is to assess patient adherence to anti-tuberculosis treatment on DOTS regimen and factors that affect adherence.
Methods: In this study both quantitative methods was used. For the quantitative method the records of a cohort of patients were followed retrospectively to see the treatment outcome; patient registration book from January 2007 to June 2010 was reviewed.
Result: out of 1050 patients enrolled in the study 207(21.6%) of patients were non adherent and 188(90.82%) of the non-adherent patients were in the continuation phase of treatment. Patients outside 10km radius were 3.423 times non adherent than TB patients living in Dessie town and within 10km radius.
Conclusion: Patients' decisions to stop taking medication were influenced by a number of interacting factors. Adherence to the long course of tuberculosis treatment is a complex, dynamic phenomenon with a wide range of interacting factors impacting on treatment taking behavior. The findings of this study could help inform the development of patient centered interventions and of interventions to address structural barriers to treatment adherence. It has been seen also that the non-adherence rate of this study setting is high, and the main determinant factors of treatment non adherence are address and HIV status of the patient.

Key words: Adherence, Tuberculosis, Ethiopia

3/28/2015 **Source of Support:** Nil, **Conflict of Interest:** None Declared

How to Cite: Kahissay MH. 2015. **Assessment of Patient Adherence to Tuberculosis Treatment in Dessie Referral Hospital, South Wollo, Ethiopia** *Malaysian Journal of Medical and Biological Research*, 2, 16-27.

INTRODUCTION

BACKGROUND INFORMATION

TB is a major public health problem throughout the world. According to the WHO Global Report 2007, one-third of the world's population is estimated to be infected with tubercle bacilli and hence at risk of developing active disease. Globally, in 2005, the annual incidence of TB, expressed as the number of new TB cases, was about 8.8 million people (7.4 million of these in Asia and sub-Saharan Africa), and the annual number of deaths due to TB was 1.6 million, including 195,000 patients infected with HIV (MOH, 2005). Tuberculosis is a major contributor to the global burden of disease and has received considerable attention in recent years, particularly in low- and middle-income countries where it is closely associated with HIV/AIDS. Poor adherence to treatment is common despite various interventions aimed at improving treatment completion. Lack of a comprehensive and holistic understanding of barriers to and facilitators of treatment adherence is currently a major obstacle to finding effective solutions (Munroet.al, 2007). Tuberculosis is almost always curable if patients are given sufficient uninterrupted therapy. Despite the treatability of this infection, however, tuberculosis has proved impossible to eliminate and the number of drug-resistant cases has increased (Chaulk and Kazandjia, 1998).
Tuberculosis has been recognized as a major health problem in Ethiopia. Though control efforts started in the early 1960s, its impact in curing the magnitude of the problem was insignificant (Mesfinet.al, 2005). In the year, 2006/7 Ethiopia registered 129,743 cases of TB. According to latest estimates, Ethiopia stands seventh by estimated number of cases among the 22 TB High Burden Countries (MOH, 2005, WHO 2005).The burden of tuberculosis is increasing despite the introduction of DOTS strategy (Mesfinet.al, 2005). Although other countries started DOTS as early as 1985, Ethiopia introduced DOTS strategy in 1993 with its gradual expansion to all parts of the country (Mesfinet.al, 2005,CDC, 1993).
Patient non-adherence has been identified as the most serious problem in tuberculosis control. In some areas the rate of non-adherence accounts nearly 50%. The DOTS strategy was introduced with aim to increase patient adherence to treatment and ensure that patients are taking their treatment (Chaulk and Kazandjia, 1998).

STATEMENT OF THE PROBLEM

The consequences of non-adherence to treatment include increased rates of treatment failure, relapse, acquired drug resistance, and prolonged infectiousness of patients (Weis et.al, 1994, Burman et.al, 1997). Therefore effective treatment of tuberculosis requires adherence to a minimum of 6 months treatment with multiple drugs. To improve adherence and cure rates, directly observed therapy is recommended for the treatment of pulmonary tuberculosis (Robert et. al, 2004). It is known that the presence of MDR TB in Ethiopia accounts 1.6% and 11.8% in new cases and retreatment cases respectively. This indicate that the presence of adherence problem (FMOH, 2008).

Defaulting from treatment remains a challenge for most tuberculosis programs. A study conducted in Hosanna Hospital shown that 20% of patients on treatment were defaulters (Biru and Bernt,2007). Unpublished report from Amhara Regional health bureau shows that the burden of TB in the Amahara region is also increasing from time to time. That is the number of cases are 27332 in 2005, 23458 in 2006, 28556 in 2007, 30074 in 2008, and 31635 in 2009. This shows the gradual increase of the reported cases. Case detection and cure rate in the Region is far below the target assigned in MDG 6 i.e. in average about 21.6% and 70.2% respectively (in between 2005 – 2009) (ANRSHB, 2009).

On the other hand MDR-TB is a newly emerged challenge in Ethiopia. WHO estimated that about 5000 new MDR-TB infections annually (Ethiopia, 2010).Therefore there is a research gap to assess the anti-TB drug adherence and factor contributing to non-adherence in Ethiopia.

LITERATURE REVIEW

BURDEN OF TUBERCULOSIS

Global Burden

TB is a major public health problem throughout the world. According to the WHO Global Report 2007, one-third of the world's population is estimated to be infected with tubercle bacilli and hence at risk of developing active disease (MOH, 2005). Tuberculosis is a major contributor to the global burden of disease and has received considerable attention in recent years, particularly in low- and middle-income countries where it is closely associated with HIV/AIDS. Worldwide an estimated 8·8 million new cases of tuberculosis resulted in 1·7 million deaths were registered and 27% of these cases and 31% of these deaths arose in Africa, home to only 11% of the world's population (Elizabeth, 2006). The study conducted in Latvia shows that from 1991 until the end of 1998 the number of patents with TB increased 2.5 times with a simultaneous increase of drug resistance and MDR-TB. Starting from DOTS TB in 1996 in Latvia the cure rates for TB patients increased from 59.5% in 1996 to 77.5% in 2003, between 1996 and 2003 more than 200 patients began MDR-TB treatment each year and the cure rate was between 66% and 73 % (Leimane and Leimans, 2006).

Local Burden

It is known that MDR TB in Ethiopia accounts 1.6% and 11.8% in new cases and retreatment cases respectively, this indicate that the presence of adherence problem (FMOH, 2008). Defaulting from treatment remains a challenge for most tuberculosis programs. A study conducted in Hosanna Hospital shown that 20% of patients on Treatment were defaulters. On the other hand MDR-TB is a newly emerged challenge in Ethiopia. WHO estimated that about 5000 new MDR-TB infections annually (Ethiopia, 2010). Before the introduction of DOTS in Ethiopia, 82% of TB patients were reported to have failed to complete treatment (Demissie andKebede, 1994). Unpublished report from Regional health bureau shows that the burden of TB in the Amahara region is also increasing from 27332 in2005 to 31635 in 2009.This shows that how the gradual increase of the reported cases. Case detection and cure rate in the Region is far below the target assigned in MDG 6 i.e. in average about 21.6% and 70.2% respectively (in between 2005 – 2009) (ANRSHB, 2009).

MULTI-DRUG RESISTANCE-TB SITUATION

Global and Local MDR-TB situation

The diagnosis of drug-resistance TB is still extremely low despite as many a half a million cases and 150, 000 deaths from MDR-TB in 2008 globally according to the WHO report 2008. In 2008 there were 29,432 MDR-TB cases reported throughout the world by 127 countries, but these cases represent only 7% of the MDR-TB cases estimated to have emerged at that year. The number of MDR-TB increases in Latvia and more than 200 patients began MDR-TB treatment each year (Leimane and Leimans, 2006). Africa experienced an estimated 69, 000 cases of MDR-TB in 2008. Since African countries have the highest incidence of TB per population in the world, even at low level of drug resistance the case load of MDR-TB patients become very high. As a result the rate of MDR-TB cases arising per 100, 000 population and in some southern African countries the burden of MDR-TB are 5 to 6 times higher than those of China and India. In addition treating MDR-TB can cost 50 and 200 times more than first line treatment for non-resistant cases (WHO, 2010). MDR-TB is a newly emerged challenge in Ethiopia. WHO estimated that about 5000 new MDR-TB infections are registered annually?

PROBLEM OF ADHERENCE

Poor adherence to treatment is common despite various interventions aimed at improving treatment completion. Lack of a comprehensive and holistic understanding of barriers to and facilitators of, treatment adherence is currently a major obstacle to finding effective solutions (Munroet.al, 2007). The official completion rate in the country (district) was 91.6%, whereas the completion rate during the study from the analysis of records, which was in part prospective, indicated the most optimistic completion rate proxy for new cases was 74.1% (percentage of new patients starting treatment who visit on month 5 for their last month's treatment), with only 50.3% attending the final visit at 6 months. (Daiyu et.al, 2008) Patients treated by directly observed therapy at the start of therapy had a significantly higher cure rate compared with patients treated by self-administered therapy, with treatment completion of 97.8% versus 88.6%. But rates of treatment failure, relapse, and acquired drug resistance were similar between the two groups. Whoever 44% of patients who received self-administered therapy had risk factors for non-adherence and should have been assigned to directly observed therapy (Robert et. al, 2004).

Therapeutic regimens recommended by WHO have been shown to be highly effective for both preventing and treating TB, but poor adherence to anti- TB medication is a major barrier to its global control. TB is a communicable disease, thus poor adherence to prescribed treatment increase the risk of morbidity, mortality and drug resistance at both individual and community level. Generally the compliance of patients decrease with time and it is lower in long–term medication than in short-term medications. It is true that the possible factors of non-compliance may vary from country to country and may contribute to the variation that exists (Diwan and Thorson, 1999). DOTS (formerly standing for Directly Observed Treatment, Short-course) are the internationally recommended control strategy for TB. This strategy includes the delivery of a standard short course of drugs, lasting six months for new patients and eight months for retreatment patients, to all those diagnosed with TB. The delivery includes the direct observation of treatment taking (DOT), either by a health worker or by someone nominated by the health worker and the patients for this purpose (sometimes called a DOT supporter). The strategy has been promoted widely and implemented globally. Up to half of all of patients with TB do not complete their treatment (Volmink and Garner, 2006).Patients who had missed 10% of their total prescribed doses of TB drugs were considered to be non-adherent. The study carried out in China showed that the non-adherence rate was 12% (Danielet.al, 2006). Another study showed that there were 23% of defaulting cases. Defaulting rate was highest (78.1%) during the continuation phase of the treatment (Marais et.al, 2006). In the southern region of Ethiopia DOTS was introduced in 1996. An earlier study on the impact of DOTS in the Southern Nations Nationalities and peoples' Regional state reported a significant declining trend in treatment non completion (non-adherence) from 38% to 18% over six years during 1994–2000 (Shargie and Lindtjorn, 2005).

COMPLICATION OF NON-ADHERENCE

Since the magnitude of non-compliance with medications prescribed for patients with chronic illness such as TB, hypertension, asthma, diabetes and epilepsy ranges between 16.7% and 80% (ATS, 2003). Therefore DOT is the cornerstone of a patient-centered approach of treatmentto maximizes the likelihood of completion of therapy. Efforts to improve treatment outcomes require better understanding of the particular barriers to and facilitators of adherence to TB treatment, and patient's experience of taking treatment. Treatment non adherence contributes to prolonged infectiousness, drug resistance, relapse and death (WHO, 2003).

POSSIBLE CAUSES OF NON-ADHERENCE

The difficulty experienced by patients following a particular treatment regimen has raised awareness of adherence as a complex behavioral issue, influenced by many factors including gender and the impact of HIV. WHO has attempted to classify factors that influence adherence to TB treatment based on a cursory review of key papers. (Xu et.al, 2009)

The main reasons for loss to follow-up (non-adherence) were: migration, unemployment, address or telephone number change, death, and refusal to join the study. (Danielet.al, 2006)

HIV positive patients have twice the risk of defaulting during the intensive phase of the treatment than HIV-negative patients (OR 2.62: CI 0.84 – 7.97, p= 0.06). The main risk factors which affect treatment compliance are sex, and previous treatment. (Marais et.al, 2006)

The study conducted in cape Town, South Africa, from January 1996 to September 2003 shows that adherence to anti TB treatment was significantly better than adherence to chemoprophylaxis (82.6%vs 44.2%). And adherence to a 3 months chemoprophylaxis regimen of Isoniazid (H) and Rifampicin, (combination 3HR) was significantly better than adherence to a 6-month chemoprophylaxis regimen of Isoniazid only (69.6% VS 27.6%)(Fredrick et.al, 2004). Another study conducted in Ndola Zambia shows that 29.8% of the patients stopped taking their medicine at two months after commencing treatment. Factors associated with defaulting in this study, include patients beginning to feel better, lack of knowledge on the benefits of completing a course, running out of drugs at home and TB drugs being too strong to continue. However, the major and striking determinant of non-compliance was

patients beginning to feel better. The rate of non-compliance to take the prescribed drug is more in female than male with a rate of 39.1% and 33.9% respectively (Gemberu, 2000).
A study done in Agaro town, Ethiopia, shows that from 37.5% defaulter from treatment 52.8%were males and 47.2% were females (Getinet, 2005). While study conducted in Gondar shows that the overall compliance rate was 73.9% and the remaining 26.1% of the patients failed to comply with clinical prescriptions (Abule, 2000).

SIGNIFICANCE OF THE STUDY

Despite the invention of effective drugs for the treatment of TB before a long period and the introduction of DOTS,TB still become a global problem especially in developing countries including Ethiopia. Since TB affects the most economically productive age groups especially in the era of HIV/AIDS, the burden exacerbate especially in poor countries like Ethiopia. Moreover, TB is the most communicable disease and global problem especially in developing countries including Ethiopia and the emergence of MDR-TB imposes a significant problem in the control of TB; little is done on the treatment of TB and patient adherence to anti-TB treatment.
In Ethiopia there was no much effort done before regarding patient adherence to anti-TB treatment, therefore little is known about patient adherence on TB treatment, so that this study could help to know the status of patient adherence and factors that affect adherence in the study area and serve as baseline study for future assessment of patient adherence to anti-TB treatment.
Since the burden of TB in the Region is increasing from time to time, this study will give information to the policy makers about the situation of TB treatment adherence both to the country and the Region.

OBJECTIVES OF THE STUDY

General objective is to assess treatment adherence rate and its determinants in TB- patients on DOTS program in Dessie Referral Hospital. The specific objectives are:

- To determine the treatment adherence rate of TB patients on DOTS program.
- To identify determinant factors of adherence in TB patients on DOTS program.

METHODS

STUDY AREA AND PERIOD.

TB patients registered for treatment in Dessie referral hospital from January 2007 to June 2010 were included. Dessie Referral hospital is found in Dessie town. Dessie town is located 400 Km away from the capital city of Ethiopia (Addis Ababa) in Amahara National regional state, North east Ethiopia. It is a hospital which provides several health services for the community and one of the institutes in which DOTS program is implemented for many years. There were about 2415 patients on DOTS Program since 2007. The hospital serves both as basic service unit for patients to its catchment area and as a referral hospital for the population of Amahara National regional state especially North and South Wollo, Oromia Zone and adjacent region (Afar National Regional state).

STUDY DESIGN

A retrospective cross-sectional study where conducted by a cohort of TB patients who were longitudinally followed to check their treatment outcome. The study utilized Quantitative methods for data collection. For Quantitative method patient registration book from DOTS clinic was used retrospectively. Using data collecting format, number of defaulters and treatment interrupters, types of TB, card number, address, sex, treatment outcome and co-morbid illness were collected. The association with patient adherence was assessed using SPSS version 16.0 for windows using chi-square and Odds ratio and epi Info for data entry.

POPULATION AND SAMPLE

Source population: All registered Tuberculosis (TB) patients lived in Dessie Town and its surroundings.
Sample population: Registered TB patients during the time period between January1st 2007 and June 30, 2010who have been on DOTS regimen at Dessie Referral Hospital.

SAMPLING TECHNIQUES AND SAMPLE SIZE

Tuberculosis patients registered between January1st 2007 and June 30, 2010 in Dessie referral Hospital were taken and some socio-demographic characteristics of TB patients (age, sex and address), type of TB, treatment defaulter, defaulting period, treatment interrupter co-morbid illness (HIV status of the patient) and treatment outcome were collected from patient registration book using two druggist.

Sample size

The sample size of the study for the quantitative method was calculated using margin of error (w) = 3% and proportion (p) = 50% (0.5) and 95% CI, even though there are many studies on this regard I have preferred to use

50% prevalence and 3% of margin of error. Which gave the sample size of 1068 and a 10% contingency was included and become 1175, using the formula

$$N = \frac{(Z\alpha/2)2p(1-p)}{W^2} = \frac{(1.96)\ 2 \times 0.5(1-0.5)}{(0.03)^2}$$

$$= 1067.111 \approx 1068$$

Unfortunately during the study period January 2007 to June 2010 the numbers of TB patients who have follow up and registered in Dessie Referral hospital were 1050.

For the qualitative method 12 patient on DOTS and 2 providers were purposively selected to have in-depth interview on possible causes of patient non adherence to TB treatment. And the sample size was determined based on the point of saturation (redundancy) and conducted by one Nurse and one pharmacist from December 1st 2010 to January 16 2011 using semi-structured in-depth interview guide.

Inclusion and Exclusion criteria

The inclusion criteria document review was being a TB-infected and being on treatment in the study site during the period of January 1, 2007 to June 30, 2010.

The exclusion criteria for Qualitative study was being a TB-infected person < 15 years of age; under DOTs treatment; and not being a current patient at study site.

MEASUREMENT

Variables: Dependent Variable was Adherence rate and the Independent variables were: Socio demographic characteristic of patients (Age, Sex, and Address); Duration of treatment; Co-morbid illness; Type of TB (PTB+, PTB, EPTB); HIV status of the patient

Data Collection: The data abstraction format was used to collect data from tuberculosis patient-registration book. After completing study material and getting permission from the concerned body, selection and training of data collector and supervisor were performed. The data collectors were one Nurse and two druggists who have training on dispensing of anti-TB (DOTS regimen), the principal investigator was supervising the data collection processes. The data collection training was conducted using a pre-test of the questionnaire as part of the training with the guidance of principal-investigator.

DATA PROCESSING AND ANALYSIS:

EPI-Info version 6.04 and statistical package for social sciences (SPSS) version 16.0 programs were used for quantitative data entry and analysis respectively. All the data collected was checked for accuracy and completeness prior to entry in to the data base. After the data entry, the data base information cross-checked with the data collection forms before commencement of analysis.. Presentation of data was in the form of tables. Data entry person recruited to enter all data collected from the area.

DATA QUALITY ASSURANCE

Training was given to the data collectors and questionnaire was pre–tested and consistent supervision of data collector was carried out.

OPERATIONAL DEFINITIONS

Adherence: Adherence to any regimen reflects behavior of one type or another, seeking medical attention, filling prescriptions, taking medication appropriately, obtaining immunization, attending follow up appointment and executing behavioral modifications, relationship between the patient and the health care provider (be it physician, pharmacist, nurses or other health practitioner) must be a partnership that draws on the abilities of each.

Non adherence: A patient said to be non-adherent if he/she missed 10% of the total prescribed drugs.

Cure: A initially smear-positive patient who is sputum smear-negative at, or one 'month' prior to, the completion of treatment and on at least one previous occasion (Usually at the end of the 2nd or 5th month).

Treatment completed: A patient who completed treatment but for whom smear results are not available at 7th month or one month prior to the completion of treatment.

Treatment failure: A patient who remains or becomes again smear-positive at the end of 5 "month" or later during treatment. Or a patient who was PTB-negative at the beginning and turned out smear-positive at the end of the intensive phase.

Defaulter: A patient who had been on treatment for at least 4 weeks and whose treatment was interrupted for 8 or more consecutive weeks.

Interrupter: A patient who discontinue his/her treatment between 4 weeks and 8weeks.

Smear-positive pulmonary TB (PTB+): A patient with at least two initial sputum smear examinations positive for AFB by direct microscopy, or a patient with one initial smear examination positive for AFB by direct microscopy and culture positive, or a patient one initial smear examination positive for AFB by direct microscopy and radiographic abnormalities consistent with active TB as determined by clinician.

Smear-negative pulmonary TB (PTB-): A patient having symptoms suggestive of TB with at least 3 initial smear examinations negative for AFB by direct microscopy, and no response to a course of broad-spectrum antibiotics, and again three negative smear examinations by direct microscopy, and radiological abnormalities consistent with pulmonary tuberculosis Decision by a clinician to treat with a full course of anti- tuberculosis or a patient whose diagnosis is based on culture positive for mycobacterium tuberculosis but three examinations negative by direct microscopy.

Extra-pulmonary TB (EPTB): TB in organs other than the lungs, proven by one culture-positive specimen from an extra- pulmonary site or histo-pathological evidence from a biopsy, or TB based on strong clinical evidence consistent with active EPTB and the decision by physician to treat with a full course of anti-TB therapy.

Ethical Consideration

Ethical Clearance was obtained from ethical clearance committee of School of pharmacy, Addis Ababa University and South Wollo Zone health office. For the in-depth interview verbal consent was obtained from every respondent after explaining the purpose and before proceeding to the interview. Privacy during interview process and Confidentiality of the data collected was kept.

Result

Patient register was reviewed for patients enrolled from January 2007 to June 2010. A total of two thousand four hundred fifteen TB patients were registered as new cases for treatment in Dessie Referral Hospital TB follow up clinic during this period. Among 2415 TB patients 1365 (56.52%) were transferred out to different Health institution and 1050 (43.48%) had treatment follow up in the Hospital therefore included in the analysis. Whereas 47(3%) of TB patients were on treatment and included in the study, 75 (7.8%) were died and 92 study subjects were missing (i.e. their treatment outcome is not known). In general 81.5% of the sample size was enrolled in the study. The age of the patients as shown in table 1 ranges from 1 to 85 years and the median age was 25years.

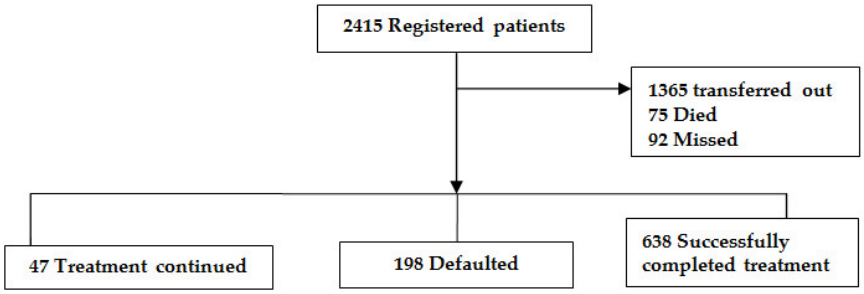

Figure 1: TB patients registered as new cases for treatment in Dessie Referral Hospital TB follow up clinic during January 2007 to June 2010(study profile)

Socio-Demographic Characteristics of Patients

Table one shows the socio demographic distribution of TB patients enrolled in the study. From the1050 cases included in the study 880 (83.8 %) of the patients who were affected by TB are the most productive age group and 828 (78.9%) were from Dessie and within 10km radius. This shows that most of the patients who got diagnostic service in Dessie Referral Hospital transferred out to their respective residence which coincides with the principle of MOH Ethiopia, i.e. every TB patient should get his/her treatment at the nearest health institution of his/her residence.

More males are affected by TB than females 58% (n=609) and 42% (n=441) respectively with male to female ratio of 1.38:1. Even though more males are affected by TB than females the difference is not statistically significant p=0.122. The rest of the result can be observed from table 1.

Table 1: Socio-demographic Distribution of TB patients in Dessie Referral Hospital from January 2007 to June 2010(N=1050)

		Frequency	Percentage
	0-14	129	12.3
	15-24	365	34.8
	25-34	302	28.8
	35-44	153	14.6

Age Group	45-54	60	5.7
	55-64	25	2.4
	65-85	16	1.5
	Total	1050	100
Gender: Male		609	58.0
Female		441	42
Total		1050	100
Address: Near		828	78.9
Far		222	21.1
Total		1050	100

Distribution of TB Patients by Type of TB, Age Group, Gender, HIV Status and Address

Almost equal proportion of the population is affected by EPTB and PTB- with a ratio of 1:0.86 the rest are affected by PTB+. Out of the study subject's 154(14.7%) were PTB positive, 413(39.3%) were PTB negative and the rest 483 (46.0%) were extra pulmonary tuberculosis. The HIV status of the study shows that 294(28.0%) were HIV positive , 336(32.0%) were HIV negative and the rest 420(40.0%) of the patients were no tested for HIV , but the proportion of HIV positive patients may be different from what have been shown on table 2 if all TB patients were willing to be tested for HIV.

The association of age and the prevalence of TB is statistically significant with a p-value of <0.001 and being HIV+ make more susceptible to TB than HIV- p= 0.005

Table 2: Distribution of TB patients by type of TB, Age group, Gender, HIV status and Address in Felegehiwot Referral Hospital between January 2007 and June 2010(N=1050).

		Type of TB			Total No.	P-Value
		PTB+No (%)	PTB-No.(%)	EPTB No.(%)		
Age group	0-14	3 (2.3)	56(43.4)	70 (54.3)	129	P< 0.001
	15-24	73 (20.0)	126 (34.5)	166 (45.5)	365	
	25-34	54 (17.9)	122 (40.4)	126 (41.7)	302	
	35-44	13 (8.5)	68 (44.4)	72 (47.1)	153	
	45-54	6 (10.0)	24 (40.0)	30 (50.0)	60	
	55-64	2 (8.0)	9 (36.0)	14 (56.0)	25	
	>65	3 (18.8)	8 (50.0)	5 (31.2)	16	
	Total	154 (14.7)	413(39.3)	483(46.0)	1050	
Gender	Male	92(15.1)	253(41.5)	264(43.3)	609	P= 0.122
	Female	62(14.4)	160(36.3)	219(49.7)	441	
	Total	154(14.7)	413(39.3)	483(46.0)	1050	
HIV status	HIV-	53(15.9)	122(36.4)	161(47.8)	336	P =0.005
	Non tested	67 (16%)	153(36.43%)	200(47.62%)	420	
	HIH+	34(11.6)	138(46.9)	122(41.5)	294	
	Total	154 (14.7)	413(39.3)	483(46.0)	1050	
Address	Near	141	339	348	828	P =0.036
	Far	13	74	135	222	
	Total	154	413	483	1050	

Chi-square

Distribution of Treatment Outcome, Type of TB and HIV Status among TB Patients

Out of 1050 TB patients the treatment completion rate was 66.6% (n= 638), (113(11.8%) cured, 525(54.8%) treatment completed) while 47(4.9%) were on treatment, 9(0.9%) patients were interrupted their treatment for one month at different time during their treatment and then continued their treatment and 198(20.7%) patients were defaulted their treatment more over 92(9.6%) of patients were missing since their treatment outcome is not known.

Regarding the treatment outcome, type of TB and gender have no association with the death of TB patients, p= 0.382 and 0.275 respectively and gender and age have no association with treatment defaulter with a p-value of 0.929, OR = 0.973, 95%CI = 0.708-1.337 and 0.089 respectively. HIV status of TB patient has strong association both with death of patient due to TB and treatment defaulter p<0.001, OR = 3.652 with 95%CI = 2.264-5.889 and p = 0.014, OR = 1.518 with 95% CI = 1.087-2.121

Table 3: Distribution of Treatment outcome, type of TB and HIV status among TB patients in Dessie Referral Hospital between January 2007 and June 2010 (N =1050).

		Treatment Outcome						
		Cured	Completed	Defaulted	Died	Continue	Missed	Total
		Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	
Age group	0-14	3 (2.3)	74(57.4)	24(21.1)	6 (4.7)	7 (5.4)	15	129
	15-24	58 (15.9)	189(51.8)	62(18.2)	15(4.1)	17 (4.7)	24	365
	25-34	36 (11.9)	148(49)	55(19.9)	27 (8.9)	10 (3.3)	26	302
	35-44	10 (6.5)	76(49.7)	36(24.5)	17(11.1)	8 (5.2)	6	153
	45-54	3 (5.0)	26(43.3)	11(22)	5 (8.3)	5 (8.5)	10	60
	55-64	1 (4.0)	6(24)	7(41.2)	3 (12.0)	0 (0.0)	8	25
	65-85	2 (12.5)	6(37.5)	3(23.1)	2 (12.5)	0 (0.0)	3	1316
	Total	113 (11.8)	525(54.8)	198(20.7)	75 (7.8)	47 (4.9)	92 (8.8)	1050
Gender	Male	68 (11.2)	308(50.6)	117(20.9)	48(7.9)	20 (3.3)	48	609
	Female	45 (10.2)	217(49.2)	81(20.4)	27(6.1)	27 (6.1)	44	441
	Total	113 (11.8)	525(54.8)	198(20.7)	75(7.8)	47 (4.9)	92 (8.8)	1050
HIV status	HIV+	19 (6.5)	126(42.9)	69 (25.8)	42(14.3)	11 (3.7)	27	294
	HIV-	42(12.5)	177(52.7)	57(17.0)	15(4.46)	16 (4.76)	29	336
	Non tested	52(12.38)	222(52.86	72(17.14)	18(4.29)	20(4.76)	36	420
	Total	113 (11.8)	525(54.8)	198(20.7)	75 (7.8)	47 (4.9)	92 (8.8)	1050
Type of TB	PTB+	113 (11.8)	0 (0.0)	20 (13.2)	15 (9.7)	3 (1.9)	3	154
	PTB-	0	241(58.4)	91 (23.9)	30 (7.3)	18 (4.7)	33	413
	EPTB	0	284(58.8)	87 (20.4)	30 (6.2)	26 (6.1)	56	483
	Total	113	525(54.8)	198(20.7)	75 (7.8)	47 (4.9)	92 (8.8)	1050

Distribution of Defaulter among Defaulting Period and Treatment Interruption

Among the defaulter 179(90.4%) were defaulted in the continuous phase, but from the treatment completion part only 9 (1.2%) of TB patients were interrupted their treatment during the treatment and taken their medication after one month and completed full course of treatment. As indicated in the operational definition. Treatment interruption of the patient increases the non-adherence rate by 4.35% while the defaulter accounts about 95.65% of the total non-adherence rate.

Table: 4 Distribution of Defaulter among Defaulting period and Treatment interruption for one month in Dessie Referral Hospital between January 2007 and June 2010.

		Treatment Interruption for less than two months		Defaulting period	
		No	Yes	Intensive phase	Continuous phase
Defaulter	No	751 (98.8)	9 (1.2)	0	0
	Yes	198 (100)	0	19 (9.6)	179 (90.4)

Factors Predicting Anti-TB Treatment Adherence

Table 5 shows that most of the independent variables have no association with patient adherence either looking at crude odds Ratio or Adjusted Odds Ratio. But some variables have association with patient adherence.

Patient address and HIV status of the patient have association with patient treatment adherence with p <0.001 and p <0.008 respectively. But the deferent variables have some difference strength in their association with treatment adherence, i.e. patients whose residence is outside 10km radius are more reliable being non-adherent (3.423x) than that of patients living in Dessie and within 10km radius.

Table: 5 Factors predicting Anti-TTB Treatment Adherence Using Logistic Regression

		Adherence		COR (95%CI)	AOR(95%CI)	P-Value	
		Adhered	Not adhered				
		No.(%)	No.(%)			Crude	Adjusted
Age group	0-14	90(78.1)	24(21.1)	1	1		
	15-24	276(80.9)	65(19.1)	.883(.522-1.493)	1.357(.776-2.374)	.643	.284
	25-34	217(78.6)	59(21.4)	1.02(.598-1.74)	1.198(.677-2.119)	.943	.535
	35-44	110(74.8)	37(25.2)	1.261(.70-2.26)	1.389(.750-2.574)	.436	.296
	45-54	38(76.0)	12(24.0)	1.184(.54-2.61)	1.24(.565-2.945)	.675	.546
	55-64	10(58.8)	7(41.2)	2.625(.90-7.62)	2.946(.990-9.072)	.0.076	.052
	65-85	10(76.9)	3(23.1)	1.125(.287-4.41)	1.414(.342-5.847)	.866	.62
	Total	751(78.4)	207(21.6)				
Gender	Male	438(78.1)	123(21.9)	1	1		
	Female	313(78.8)	84(21.2)	.956(.699-1.307)	.876(.630-1.22)	.776	0.432
	Total	751(78.4)	207(21.6)				

Address	Near	658(82.1)	143(17.9)		1		
	Far	93(59.2)	64(40.8)	3.167(2.19-4.57)	3.423(2.32-5.05)	<.001	<0.001
	Total	751(78.4)	207(21.6)				
Type of TB	PTB+	129(85.4)	22(14.6)	1	1		
	PTB-	284(74.7)	96(25.3)	1.982(1.19-3.29)	1.749(1.036-2.95)	0.008	0.365
	EPTB	338(79.2)	89(20.8)	1.544(.93-2.57)	1.275(.752-2.16)	0.094	0.367
	Total	751(78.4)	207(21.6)				
HIV status	No HIV	557(80.6)	134(19.4)	1	1		
	HIV+	194(72.7)	73(27.3)	.639(.460-.888)	1.637(1.14-2.35)	0.008	0.008
	Total	751(78.4)	207(21.6)				

DISCUSSION

This study tried to measure treatment adherence of TB patients and identifies factors that affect adherence. Approximately a total of one –fifth of patients included in the study became non adherence to their treatment. Even though there is some irregularities in the decrement of non-adherence, this finding confirms an earlier study report that showed a decrease in defaulter (non-adherence) rate from 38% to 18% over a six year period from 1994 to 2000 (Getinet, 2005). The treatment adherence rate of this study was 78.4% or the non-adherence rate was 21.6% which is higher than the finding in a study done in Hosanna Hospital (Biru and Bernt, 2007). But on the other hand the non-adherence rate of this study is lower when compared with findings in some part of the world like China, some European and many African countries (CDC, 1993; Shargie and Lindtjorn, 2005). And even this finding is lower than the findings in other part of the country (Fredrick et.al, 2004). But in general the treatment adherence rate and the treatment success rate of this study are lower than the treatment success rate (85%) set by the Millennium Development Goals (Gemberu, 2000).

In this study the treatment completion rate of the patient after the exclusion of the death cases is 72.25% which is far from the treatment success rate set by the millennium Development Goals(y). As observed from the result TB is highly (83.8%) affected the most productive age group which coincides with some findings and truth of the world (10, 11). Age and HIV status of the patient are associated with the prevalence of TB with a p-value <0.001 and p= 0.005 respectively. While more males are affected by TB than females (58% and 42% respectively), but this difference is not statistically significant with a p-value = 0.122.The probable reason for this result may be males have more contact to different people and they are more mobile than females so they may have more contact with TB patients and this result is similar with other study (WHO, 2003). Most of the independent variables used in this study have no association with treatment adherence except address and HIV status of the patient with $p < 0.001$, and $p = 0.008$ respectively. Since the study was conducted using only patient registration book without tracing the non-adherent patients; rather if the study is conducted by tracing the non-adherent patients there may be a number of factors that may associate with treatment non adherence like (socio-economic status, knowledge of TB disease and the benefit of treatment completion of the patient, side effect of drugs, patient-provider interaction and others (Biru and Bernt, 2007; Daniel, 2006). So further investigation is very essential to put forward solution.

The burden of death due to TB in the world is high. Even though the death rate of this study is 7.8% this may not be the actual death rate since the study was conducted only based on patient registration book and there is a problem of tracing the non-adherent patients based on this assumption the death rate may increase due to the possibility of more deaths among patients who were non adherent to their treatment (WHO, 2005). On the other hand there were 5 patients who were reported as treatment failure out of 1050 study subjects enrolled in the study both form registration book and in the in-depth interview and sat on retreatment (Biru and Bernt, 2007). Though they are on retreatment the treatment failure may lead to the development of drug resistance and consequently to the development of MDR- TB which is the problem of the world including Ethiopia (Shargie and Lindtjorn, 2005).

In this study 92.4% the defaulters and 92.75% the non-adherent patients were in the continuation phase of the treatment especially in the 3rd and 4th months of the treatment. The most probable reason, as discussed in in-depth interview, why patients default or become non adherent to their treatment are during these period most of the symptoms disappear and patients may wrongly understand that they are cured. This may initiate the patients to become unwilling to continue their treatment correctly. In addition the HIV status of the patients also contribute a lot for the non-adherent rate of the treatment(35.27%) from only 267 HIV+ cases though 27 HIV+ patients were missed. The other reason for treatment non adherence the patient can the length of TB treatment since most of the treatment non adherence were in the continuation phase (Shargie and Lindtjorn, 2005; Daniel et. al, 2006; Marais et.al, 2006).

Even if most of the patients diagnosed in Dessie referral hospital whose residence is outside 10km radius were transferred out, but the treatment non adherence rate of patients whose residence is outside 10km radius accounts 31% only with 222 patients in this area. So attention should be given for the residence of patients i.e. distance from the health institution is the most associating independent variable with treatment non adherence.

Based on the translated themes and secondary interpretations, I developed a model to depict my understanding of the main influences on adherence. Components of the model include structural, personal and health service factors influencing adherence, as well as social context. I have presented structural factors and health service factors separately, instead of as a single "health systems" category, because I felt that some interventions could be directed towards wider society-level factors while others could intend to influence the person and the health service.

Structural factors: poverty, gender and discrimination

Factors such as gender and poverty determine individual responses to treatment and subsequent behavior; and they interact with a patient's social context, their personal characteristics and the health service. TB programme managers frequently assume that a willingness to adhere must be instilled in patients in order to improve adherence rates. This study has found that even where patients are willing to adhere, structural factors such as poverty and gender discrimination may prevent them from doing so. It is recognized that incorporating patients' views in medical practice often obscures the real constraints on agency that some patients experience (Farmer, 1997). In our study, structural factors were discussed in various ways, with poverty remaining one of the most important of these for treatment taking, especially when linked to health service factors, such as poorly accessible, poorly equipped and distant clinics. Our findings support the assertion that interventions to increase adherence should focus not only on the patient but also on the wider context and the health system (Sumartojo, 1993). There is a need for a shift in perspective to give greater attention to both the social and economic environment in relation to TB infection, of which the beginnings can already be seen in the international policy arena.

Patient factors: motivation, knowledge, beliefs and attitudes and interpretations of illness and wellness

Patient choice in taking treatment is framed by the physiological and psychological impacts of the disease and also by the social and cultural structures in which the person is immersed (Lienhardt, 2003). Patient motivation and willingness, and the effect of incentives on treatment taking, have received some attention (Tulsky, 2004). However, it remains unclear whether the incentive, or the attention received by the patient, serves as the primary source of motivation. Caution should therefore be exercised when attributing adherence solely to "personal motivation" (De Vos, 2002), because not only can important influences be ignored, but this factor is difficult to modify or even operationalize.

We found that personal and social factors, including poverty and social marginalization may be used by some providers to identify patients at risk of non-adherence to their medication regimen. However, it cannot be assumed that all individuals sharing a particular characteristic face the same barriers to adherence. Non-adherence can be a product of programme failures, such as an inadequate supply of drugs, rather than patient-related problems or failures (Jaiswal, 2003). Our study also found that patient Knowledge, attitudes and beliefs about TB its treatment, and patient interpretations of illness and wellness, can act as a 'filter' for the information and treatment offered by the health services. The influence of patients' interpretation of various illnesses on their adherence behavior is well documented and it is recognized that patients may interpret the themes of illness, wellness and disease differently from health professionals (Horne and Weinman, 2002), highlighting the distinctions between lay and biomedical understandings of TB (Vermeire et.al, 2001). This is unlikely to be the only influence on treatment taking, however, and patient interpretations can interact with structural and health service factors as well as with social context.

Social context

The influence of social context on treatment adherence was apparent this study. The community, household and health service helped in countering the shame and guilt that patients with TB experienced and also offered support in maintaining treatment taking. Social support can help patients overcome structural and personal barriers, and may influence their knowledge, attitudes and beliefs. Conversely, community and family members' attitudes may influence a patient's decision to stop taking TB treatment. In such circumstances, community based TB treatment programmes and stronger involvement of local social networks to support TB patients may be justified (Volmink and Garner, 2006).

Health service factors

Factors related to the provision of health services emerged strongly in this study. Flexibility and choice in treatment, and options that maintain patient autonomy in treatment taking, appeared to run contrary to the traditional organization of many TB services ((Metabesi, 2004). Directly observed treatment at a health facility often meant that a patient had to give up part of their working day to attend,(Khan et.l, 2000). However, responsibilities in the home, including providing for their family, may be given priority over treatment adherence by patients. Other health service factors, such a long waiting times and inconvenient opening times in clinics, add to economic discomfort and social disruption for patients (Klink, 1969), and negatively influence adherence. This study suggest that patients often face a choice between employment and taking medication for TB; and there is evidence that patients consciously estimate the opportunity costs of taking treatment.

STUDY LIMITATIONS

Studies often included participants from several socio-economic strata; did not always contain a detailed description of the treatment regimen; and did not explicitly consider gender in treatment adherence. The study also has the limitation of document review: difficulty to assess the reliability of the data, some data was not complete. The level of interpretation in this study was fairly basic – most were descriptive that used thematic analysis to identify key themes and did not draw extensively on theory or on a particular theoretical tradition.

CONCLUSION

This study indicates that patients often take their TB medication under difficult circumstances and experience significant challenges, many of which are outside of their direct control. Taking a lengthy course of medication is not straightforward and frequently involves difficult decisions, sometimes at significant personal and social cost to the patient. Adherence is a complex, dynamic phenomenon; a wide range of interacting factors impact on treatment taking behavior, and patient behavior may change during the course of treatment. More patient centered interventions, and far greater attention to structural barriers, are needed to improve treatment adherence and reduce the global disease burden attributable to tuberculosis. Moreover from the quantitative analysis the non-adherence rate of this study area was high, and the main factors associated with treatment non adherence are address (physical access to treatment center) and HIV status of the patients'. The continuation phase of treatment is the important time for non-adherence from treatment. The principle of adherence in the study area is not followed strictly and patients are not fully understood the benefit of DOTS.

RECOMMENDATION

- The principle of DOTS should be strictly followed in order to achieve the Millennium Development Goals.
- Patients' and contact person address should give emphasis in order to trace the non-adherent patients.
- Health education regarding TB disease and its mode of transmission and the benefit of DOTS should be given both to the patient and their families.

ACKNOWLEDGMENT

I would like to acknowledge School of Pharmacy, Addis Ababa University for funding this project. My Special thanks also go to Dr. TeferiGedif who help me in data processing and editing of the draft. I also would like to acknowledge all Tuberculosis case team members of Dessie Referral hospital for their support in data organization and shared experience for this research.

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