Full Length Research Paper

Drug adherence amongst tuberculosis patients in the University of Ilorin Teaching Hospital, Ilorin, Nigeria

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Tuberculosis is a preventable, treatable and curable disease provided the precautionary measures and drug adherence are strictly adhered to. Structured questionnaires were administered to 280 tuberculosis patients diagnosed at the Pulmonary Unit of the University of Ilorin Teaching Hospital, Ilorin, Oyo State; a tertiary healthcare centre in Nigeria. There were 166 males and 114 females giving male to female ratio of 1.4:1.0. There was a significant association between education and patients' adherence to their medications. Side effects of the anti-tuberculosis agents have negative impact on patients' drug adherence. Positive effect of counseling on the patients' adherence to their medication regimen was also recorded. Age had no significant relationship with patients' drug adherence, whereas education was significantly associated with patients' drug adherence. Drug adherence rate accounted for 94.6% of the patients seen over the period of study. The high rate of drug adherence observed was probably due to free anti-tuberculosis drugs, free medical laboratory service and the rapid improvement in the signs and symptoms of the disease. Also, directly observed treatment short course (DOTs) currently introduced in the hospital coupled with free supply of tuberculosis resistant strain drugs to patients, improved adherence and impede tuberculosis transmission within the community, and thereby stem the tide of the disease.

Key words: Tuberculosis, drug adherence, patients, Ilorin, Nigeria.

INTRODUCTION

Tuberculosis (TB) is the leading communicable disease among the ten cause of global mortality (Borgdorff et al., 2002). It is caused by Tubercle bacillus, known as *Mycobacterium tuberculosis*, whose host is human (WHO, 2001). One-third of the world's population is infected, while 8 million new cases emerged annually (Dye et al., 1999). About 5,000 persons were infected per day, of which 95% are from developing countries. The highest mortality rate is recorded in African region (WHO, 2004). Current trends suggest that these numbers could rise to 12 million cases and 4 million deaths, by the year 2010 (Bifani et al., 2002). Young children are likely to develop this disease after infection and are significantly more likely to develop extra-pulmonary and severe disseminated disease than adults (Walls and Shingadia, 2004).

The resurgence of tuberculosis is due to many factors including Human Immunodeficiency Virus (HIV) pandemic, poor nutrition, overcrowding, unsanitary living condition, drug barons, alcoholic drunkards, cultural impediments, stigmatization and lack of effective public enlightenment (Hamburg and Friensden, 1994). However, many patients, in particular those who have a chronic disease requiring therapy over prolonged period of time, have a tendency not to take medications as prescribed. The most serious problem hindering tuberculosis treatment and control is non-adherence of patients. It is believed to delay sputum conversion to smear negative, increase the relapse rates 5 - 6 times, and help the emergency of resistant mutant strains (Sullivan et al., 1990). However, adherence to tuberculosis treatment requires the active participation of the patient in self management of treatment and cooperation between the patient and the health care provider. The reasons for poor adherence with anti-tuberculosis chemotherapy in developing countries including Nigeria are multifaceted

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and complex. These include; the characteristics of the individual patient, social and economic factors such as the availability of drugs, communication between the patients and healthcare providers, duration and number of medications needed, side effects, cost of treatment, competing demands on time, contradictory norms or expectations of families and cultural groups as well as poor quality of the tuberculosis control infrastructure (WHO, 2006). Two major markers of this failure are the increasing incidence of tuberculosis and the rising prevalence of drug-resistant tuberculosis infection in the community (Blenkiron, 1996).

However, introduction of Directly Observed Therapy short course (DOTs) in the tertiary health institutions of Nigeria with the provision of free anti-tuberculosis drugs and medical laboratory tests has revolutionized the prognosis of patients with tuberculosis and tuberculosis infection. The goals of the drug therapy are to cure the disease and impede the transmission in the community (Iseman, 1993). The current guidelines call for the use of standard six-to-nine months regimens of drug therapy, much of which can be given twice weekly under direct observation. This regimen requires an initial phase of daily treatment for the first one to two months (30 to 60 daily doses). The ability to monitor drug concentrations for assessing patient adherence in those receiving chronic drug therapies is of significant value in preventing an exacerbation of their disease process. The present study was therefore conducted to determine the rate of adherence to anti-tuberculosis drugs amongst tuber-culosis patients under DOTs programme, with a view to ascertain their levels of adherence and factors responsible for non - adherence.

MATERIALS AND METHODS

This study was conducted at the out-patient clinic of Pulmonary Unit of University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria. A sample size of 300 patients out of the total population of the tuberculosis patients that visited the clinic was used for the study. The patients that met the inclusion criteria were selected.

Inclusion criteria

(i) The patients that have been on anti-TB drugs for more than two months, (ii) The sputum of the patient should contain Tubercle bacilli on direct smear and / or culture, (iii) The patients showing cardinal clinical features of pulmonary TB, such as chronic cough, haemoptysis, weight loss and night sweats, and (iv) Patients age range should be between 15 and 75 years.

Exclusion criteria

(i) Children below the age of 15 years, (ii) Psychiatric and prisoner patients at the hospital, (iii) Newly diagnosed patients, and (iv) Patients with co - morbidity medical / surgical conditions. Twenty patients did not meet the inclusion criteria; therefore two hundred and eighty (280) patients were interviewed. All smear-positive cases in this study were at the maintenance phase receiving

Ethambutol 15 mg/kg and Isoniazid 300 mg daily for 6 months. Patients with sputum containing tubercle bacilli at the end negative.

Research design

Research method instruments used to obtain information from TB patients were; structured questionnaires, patients' medical record folders and interview schedule. The structured questionnaires and interview guide was developed based on critical and detailed consideration of the research questions. The predesigned questionnaires were administered to patients with the following sections; (a) Demographic and socio-economic characteristics such as age, gender, marital status and education, (b) General information on TB, such as symptoms and signs of TB, (c) Drug adherence, such as anti-TB drugs counseling, side effects of anti-TB drugs, and adherence with medications. Patients' knowledge was ascertained based on the responses provided by the patients during the interview. Since patients are notorious for giving false information on treatment adherence, their medical records and clinical test results were studied to confirm adherence to therapy.

Ethics approval

Ethical approval was sought from University of Ilorin Teaching Hospital Joint Institutional Review Committee before the questionnaires were administered to the patients. Also, the consent of the patients was sought and obtained before questionnaires were administered to them.

Data analysis

Analysis of the completed questionnaires was carried out using Genstat statistical package (Genstat, 1995). The data were subjected to the descriptive statistics which involves the use of frequency distribution and percentages, while the quantitative analysis includes Chi - square and Regression analyses to quantify the degree of drug adherence to treatment on the TB patients.

RESULTS

The demographic and socio-economic characteristics of TB patients of UITH are presented in Table 1. Out of two hundred and eighty patients in the sample, 116 (59.3%) were males, while 114 (40.7%) were females. One hundred and nine (38.9%) of them were of the age range of 16-30 years, one hundred and two (36.4%) ranged between 31 and 45 years, forty nine (17.5%) between 46 and 60 years, while only twenty (7.2%) of the patients age ranged between 61 and 75 years. On the marital status, most of the patients interviewed were married (56.8%), while single, divorced and widowed were 33.9, 4.7 and 4.6% respectively. Based on the educational career, one hundred and thirteen (40.4%) had no formal education, while the majorities (59.6%) were literates. On the outcome of the patients (Table 2), most of frequent signs and symptoms presented by the patients at the first visit to the hospital were cough and weight loss (83.6%), followed by weight loss only (13.2%) and pneumonia (3.2%). Majority of the patients with   TB knowledge accounted for 76.4%, while those without such

Table 1. Demographic and socio economic characteristics of TB patients at the University of Ilorin Teaching Hospital, Ilorin.

Parameter studied	Classification	Number	Percentage (%)
Gender	Male	166	59.3
	Female	114	40.7
Age (year)	16 - 30	109	38.9
	31 - 45	102	36.4
	46 - 60	49	17.5
	61 - 75	20	7.2
Marital status	Married	159	56.8
	Single	95	33.9
	Divorced	13	4.7
	Widowed	13	4.6
Education	No formal education	113	40.4
	Primary school certificate	45	16.1
	Secondary school certificate	87	31.1
	Diploma/NCE	22	7.8
	HND/ First degree	8	2.8
	Masters and above	5	1.8

Table 2. Outcome of patients with tuberculosis at the University of Ilorin Teaching Hospital, Ilorin.

Parameters studied	Classification	Number	Percentage (%)
Symptoms of tuberculosis	Weight loss	37	13.2
	Cough and weight loss	234	83.6
	Pneumonia	9	3.2
Knowledge of patients about TB and curability of TB with anti TB drugs	Patients with TB knowledge	214	76.4
	Patients without TB knowledge	66	23.6
Side effects of anti tuberculosis drugs	Yellowish eyes	2	0.7
	Nausea and Vomiting	71	25.4
	Dark Urine	202	72.1
	Impaired vision	5	1.8
Adherence with medications	Patients who adhered	265	94.6
	Non-adherence Patients	15	5.4
Improvement in the health condition of patients while on anti TB drugs	Patients with improvement	243	86.4
	Patients without improvement	38	13.6
Patients with sputum conversion to negative within three months of therapy	Patients with negative sputum	202	72.8
	Patients without negative sputum	78	27.2

knowledge were 23.6%. However, dark urine features prominently (72.1%) as side effects of anti-TB drugs among the patients followed by nausea and vomiting (25.4%), impaired vision (1.8%) and yellowish eyes (0.7%). Majority of the patients (94.6%) adhered with their medications. On the other hand, most of the patients in the sampled population (86.4%) had improvement in their health condition while on anti-TB drugs. Furthermore, majority of the patients (72.8%) had their sputum conversion to negative within three months of therapy. Partial regression of effects of counseling on patients' drug adherence is presented in Table 3. The results showed that there is positive effect of counseling on the patients' drug adherence. However, Chi - square

Table 3. Partial regression analysis on the effects of counseling on patients' drug adherence.

	Unstandardized coefficients	Standardized coefficients	Standard error	t	Sig.
Counseling	0.057	0.059	0.058	0.978	0.329

Table 4. Chi-square analysis of association between age and patients' drug adherence.

Age (years)	Yes (%)	No (%)	Total (%)	X^2 observed	X^2 critical	df	A	p-value	Decision
16 - 30	13 (4.6)	96 (34.3)	109 (38.9)	0.824	7.814	3	0.05	0.844	Not sig.
31 - 45	11(3.9)	91 (32.5)	102 (36.4)						
46 - 60	4 (1.4)	45 (16.1)	49 (17.5)						
61 - 75	3 (1.1)	17 (6.1)	20 (7.1)						
Total	31 (11.1)	249 (88.9)	280 (100)						

Table 5. Chi-square analysis of association between education and patients' drug adherence.

Education	Yes (%)	No (%)	Total (%)	X^2 observed	X^2 critical	df	A	p-value	Decision
Non-formal Education	3(1.1)	11(3.9%)	14(5.0%)	21.281	11.071	5	0.05	0.001	Significant
Primary school certificate	15(5.4)	37(13.2)	52(18.6)						
Secondary school certificate	12(4.3)	75(26.8)	87(31.1)						
Diploma/NCE	17(6.1)	22(7.9)	39(13.9)						
HND/First degree	12(4.3)	40(14.3)	52(18.6)						
Masters and above	2(0.7)	34(12.1)	36(12.9)						
Total	61(2.19)	219(78.21)	280(100)						

analysis revealed that age had no significant relationship with patients' drug adherence (Table 4), whereas education was significantly associated with patients' drug adherence (Table 5).

DISCUSSION

Before the advent of directly observed therapy short course in the tertiary health institutions of Nigeria with the provision of free anti-tuberculosis drugs and medical laboratory tests, defaulting from treatment is one of the most important problems in the management of tuberculosis. Low adherence can result in drug resistant mutant strains (Sullivan et al., 1990) which can potentially interfere with future therapeutic option for those being treated. In the present research, out of total number of 280 questionnaires administered to TB patients, 59.3% were males and 40.7% were females, giving a male to female ratio of 1.4:1 (Table 1). This is similar to the findings of Morisky et al. (1998) who reported that 64% of the tuberculosis patients studied in California were males and from (Kehinde et al., 2006) that out of the total number of patients (2,738) studied in Ibadan, Nigeria, 62.4% were males and 37.6% females, with a male to female ratio of 1.6:1. However, majority of the patients in the study were within the age bracket of 16 - 45 years.

This result also corroborates with the work of Ige et al. (2005) in Nigeria which reported that 81.7% of the patients were in the age range between 20 and 40 years. Similarly, Aktogu et al. (1998) reported that out of 5,480 cases of tuberculosis in Turkey, pulmonary tuberculosis was common among patients of age 20 - 39 years. In India, Atul et al. (2004) found that about 80% of tuberculosis cases occurred in economically productive age group of 15 - 49 years. This is in contrary to what obtained in the United States of American where high risk of *M. tuberculosis* reflected more among the elderly (above 62 years) and less among those below 50 years of age (Cantwell et al., 1994). In this study, more than half (82%) of the age range between 16 and 45 years corresponds to the economically vibrant age bracket of the population. This implies that tuberculosis constitutes a strong economic burden, which could cripple the work force of the country. However, most of the patients were married which is in line with Ashry et al., 1997 studies in Alexandra, Egypt that 45 females out of 48 were house wives. Also, about 40% of the patients in this study were illiterates with lower levels of educational attainment. This may be as a consequence of ignorance and poor economic situation prevailing in the country. This is similar to the previous work of (Ashry et al., 1997). In Egypt, more than half (66%) of the patients were either illiterates or could just read and write.

Tuberculosis is a familiar illness and it involves symptoms. It's is not easily accepted that someone without a cough, weight loss, enlarge lymph nodes or other symptoms associated with the illness understood to be infected with tuberculosis disease (Adair et al., 1999). This was supported by the present study that the most (83.6%) common symptoms of tuberculosis experienced by the patients were cough and weight loss (Table 2). However, patients with such symptoms usually recognize the severity of tuberculosis and have higher tendency to adhere (Mousa et al., 1995). On the other hand, majority of patients were aware about TB as a transmissible disease which can be cured with drugs. This awareness was received through health talks from the public health nurses in the hospital. The patients' knowledge of TB was ascertained based on the responses of the patients. The side effects of anti-TB drugs are minor, tolerable and correctable which could encourage drug adherence by the patients.

On nausea and vomiting side effects experienced by the patients, (Fakeye et al., 1997) also suggested that the healthcare providers especially the pharmacists should emphasize always on the specific times the drug is to be taken in relation to meals. In spite of this, very rare adverse reaction on hepatoxicity induced by pyraziramide was recorded in few (0.7%) of the patients during personal interview. With respect to improvement in the health condition, majority of the patients realized that they felt much better while taking their medications strictly. Patients that take their medications in an irregular and unreliable manner are at high risk of treatment failure, relapse and development of drug-resistance TB strains. The most important instrument to diagnose pulmonary TB is direct sputum smear microscopy.

The cultures and tests are done on the sputum to help identify the bacteria that are causing an infection in the lungs. Regular sputum microscopy needs to be carried out looking for Acid Fast Bacillus (AFB) at specified interval during follow-up of the patient management. For smear positive patients, sputum tests are further performed at the end of the second, fifth and seventh month of the therapy respectively (Mousa et al., 1995). In the present study, most of the patients (72.8%) had sputum conversion to negative within three months of therapy. This is in keeping with 94.6% adherence rate observed in the population studied. In the pulmonary TB, sputum examination and culture are the most sensitive markers for the success of the treatment.

All healthcare providers need to counsel TB patients not only on the importance of taking their drugs regularly but also on the importance of completing their treatment. Poor adherence with tuberculosis treatment is more dangerous than no treatment because it may increase the risk of developing multi drugs resistant tuberculosis strains. Partial regression (Table 3) showed positive effect of counseling on the patient adherence with anti-tuberculosis agents. This means that the more counseling the patients received on drugs regimens, the better understanding

and higher chances of drug adherence. This invariably showed that, physicians in the Pulmonary Unit's efforts on counseling the TB patients had yielded better treatment adherence in the hospital. In other words, the patients were knowledgeable on their disease conditions and their drug therapy which invariably enhanced improvement in their health condition while on anti - TB drugs. This finding is synonymous with most other studies that have been carried out in Nigeria, including the study of Fakeye et al. (1997) in Ibadan, whereby, 55.6% of total number of patients adhered with instructions, while 44.4% often rarely or did not adhere at all.

Also, the pharmacotherapy approach to the treatment of tuberculosis revealed that majority of the patients took their drugs according to instructions given by either the pharmacists or physicians. High rate of adherence to medical regimen in these patients could also be due to; (i) Free drugs and free healthcare services, (ii) Once daily dosage regimen for anti-tuberculosis drugs, (iii) Mild / correctable side effects such as nausea, (iv) Clearly written instructions regarding the timing of medication, and (v) Easy accessibility to health centre. Non significant association ($P > 0.05$) of age with adherence to drug medication by tuberculosis patients recorded (Table 4) is similar to the study of Ashry et al. (1997) who reported that patients' adherence with medical instructions was not significantly affected by age.

Conversely, education was significantly ($P<0.05$) associated with drug adherence. This corroborates with the study of Fakeye et al. (1997) who reported that patients' adherence with instructions was significantly affected by education. This is also in line with Kyngas and Lahdenpeia (1999) who reported that high educational level tends to relate to good adherence among tuberculosis patients. This shows that the more educated a patient is, the better understanding of the disease state and comprehension of instructions given on drug usage, and these could enhance adherence.

Conclusion

The treatment by the Directly Observed Therapy approach is not only effective but also most cost effective way of prolonging healthy living of the people. The introduction of the Directly Observed Therapy short course has improved immensely the problem of non-adherence to medication regimen by the patients, and development of resistant strains thereby reducing the scourge of the disease.

REFERENCES

Adair R, Nwarneri O, Barnes N (1999). Health care access for Somali refugees. View of patients, doctors, nurses. Am. J. Health Behav. 4: 286-293.
Aktogu S, Yorgancioglu A, Cirak K, Kose T, Dereli SM (1998). Clinical

spectrum of pulmonary and pleural tuberculosis; A report of 480 cases. Eur Respir. J. 5: 2031-2025.

Ashry G, Ahmed MA, Mandil A, Sherif ZAR, Gad M, Sunny S (1997). Compliance with anti-tuberculosis drugs among tuberculosis patients. Eastern Mediterranean Health J. 3(2): 244-250.

Atul SP, Mehrotra P, Dhar HI (2004). Assessment of pulmonary tuberculosis in patients. Bombay Hosp. J. 46(2): 1-7.

Bifani PJ, Mathema B, Kurepina NE, Kreiswirth BN (2002). Global dissemination of the *Mycobacterium tuberculosis* W-Beijing family strains. Trends Microbiol. 10: 45-52.

Blenkiron P (1996). The elderly and their medication: Understanding and compliance in family practice. Postgrad. Med. J. 72: 667-6.

Borgdorff MW, Flalo K, Broekmans JF (2002). Interventions to reduce tuberculosis mortality and transmission in low and middle-income countries. Bulletin of the WHO (80): 217-226.

Cantwell MF, Snider DE Jr, Cauthen GM (1994). Epidemiology of tuberculosis in the United States, JAMA. 272(7): 535-539.

Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC (1999). Consensus statement. global burden of tuberculosis; Estimated incidence, prevalence and immortality by country. WHOs Global Surveillance and Monitoring Project. JAMA. 282: 677-686.

Fakeye TO, Itiola OA, Akindele OO (1997) Drug utilization in a University Community. Nig Qt. J. Hosp. Med. 1.7: 3.

Genstat (1995). Genstat 5 release 3.2. Reference manual supplement. Clarendon Press, Oxford, U.K.

Hamburg MA, Frieden TR (1994). Tuberculosis transmission in 1990's (ed). New England J. Med. 330: 1750.

Ige OM, Sogaolu OM, Ogunlade OA (2005). Pattern of presentation of tuberculosis and the hospital prevalence of tuberculosis and HIV co-infection in University College Hospital: A review of five years (1998-2002) in Afr. J. Med. Med. Sci. 34(3): 29 -33.

Iseman MD (1993). Treatment of multidrug-resistant tuberculosis. New England J. Med. 329(11): 784-791.

Kehinde AO, Olaniyi JA, Fakunle EE (2006). Extra pulmonary tuberculosis in sickle cell disease. Afr. J. Med. Med. Sci. 35: 381-384.

Kyngas H, Lahdenpeia T (1999). Compliance of patients with drugs and associated factors. 4: 823-829.

Morisky DE, Nyamathi A, Sneed CD, Liu KY (1998). Health education improves tuberculosis control. Gateway to the National of Medicine. Mar. pp. 8-11.

Mousa KL, Drousa, FG, Faragay SA (1995). Smear-positive pulmonary tuberculosis; preliminary results of a study in Alexandria and Menoufia, Egypt, 1993. Paper presented at the international epidemiogical association EMR meeting, Alexandria Egypt 9: 1-4.

Sullivan SD, Kreling DH, Hazlet TK (1990). Non-compliance with medication regimes and subsequent hospitalization: A literature, analysis and costs of hospitalization estimates. J. Res. Pharmaceut. Econ. 2: 19-33.

Walls T, Shingadia D (2004). Global epidemiology of pediatric tuberculosis. J. Infect. 48: 13-22.

World Health Organization (2001). Global tuberculosis control. World Health Organization, Geneva, Switzerland.

World Health Organization (2004). Report of global tuberculosis control: Surveillance, planning and financing. World Health Organization, Geneva, Switzerland.

World Health Organization (2006). Report of global tuberculosis control. 45th Annual Inter-science Conference on Antimicrobial Agents and chemotherapy, Washington DC.