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TREND IN TUBERCULOSIS MORTALITY IN NIGERIA

[1]Daniel, O.J. [2]Salako A.A [3]Ogunfowora O.B. [4]Oluwole F.A.

[1]Department of Community Medicine and Primary Care and [2]Department of Paediatrics, Olabisi Onabanjo University Teaching Hospital Sagamu, Ogun State Nigeria.

Correspondence/ Request for reprints: **Dr. Daniel, O.J. Dept of Community Medicine and Primary Care Olabisi Onabanjo University Teaching Hospital; Sagamu. Ogun State. Nigeria.**

E-mail: sojidaniel@yahoo.com. +2348033774418, Footline: TB, DOTS, Mortality, HIV.

ABSTRACT

Background Tuberculosis continues to cause considerable morbidity and mortality especially in sub Saharan Africa in spite of the availability of effective antimicrobial agents. This study aimed to assess the trend and factors associated with deaths in Sagamu Nigeria.

Design: A retrospective case control study of TB patients dying before completing the directly observed treatment short course (DOTS) at the Ogun State University Teaching Hospital; Sagamu.

Result: Of the 946 patients registered at the outpatient DOTS programme between January 1997 and December 2003, 53(5.6%) died before completing treatment. The death rate from tuberculosis rose from 5.4% in 1997 to 8.6% in 2003, an increase of 59.3%. HIV prevalence rate among TB patient increased from 7% to 25.2% during the same period. The highest age specific case fatality rate of 12% was in the age group 50-59 years. HIV positive status and history of previous TB treatment were significantly associated with dying during treatment. Neither sputum smear negativity nor pre-admission weight was associated with the risk of death. The median survival time from the commencement of treatment was 8 weeks. There was no significant difference in the survival time in relation to the HIV status.

Conclusion: This study has demonstrated an upward trend in mortality from TB infection which is associated with HIV co-infection and previous TB treatment failure. This calls for the strengthening of HIV and TB control measures, combined with strategies aimed at making antiretroviral drugs cheaper and more affordable for people living with HIV/AIDS in resource poor countries.

INTRODUCTION

Tuberculosis continues to cause considerable morbidity and mortality especially in sub Saharan Africa despite availability of effective antimicrobial agents. About 2 million people die from this disease annually with severe social and economic consequences. It cannot be ignored that TB is a disease of poverty with 95% of cases and 98% of deaths due to it occurring in the developing nations[1].Factors such as multi-drug resistance human immunodeficiency virus infection and delayed therapy have been implicated[2]. In several African countries, TB is still a major cause of morbidity and mortality[3,4]. HIV has been observed to be an important predictor of death in patients with tuberculosis[5,6]. Among medical in patients at the Olabisi Onabanjo university teaching hospital, Sagamu, TB accounted for 10% of medical admissions. TB was the commonest infectious disease

causing death and the third most common cause of death after cerebro-vascular accident and renal failure[7]. This study aimed to assess the trend and factors associated with deaths among patients attending tuberculosis and leprosy control centre in Sagamu, Nigeria.

MATERIALS AND METHODS

SETTINGS

The study was carried out in Sagamu Local Government area in Ogun State of Nigeria. The town is a semi-urban area with an estimated population of 200,000 people[8]. It is located about 50km from Lagos and Ibadan. The Tuberculosis and Leprosy control centre attached to the department of community medicine and primary care, Olabisi Onabanjo University Teaching Hospital is the major referral centre for the treatment of TB. The German Leprosy Relief Association (GLRA) was responsible for the provisions of free drugs for the programme. The centre provides DOTS for the treatment of tuberculosis on out- patient basis

TB CONTROL PROGRAMME

Patients with suspected or confirmed diagnosis of TB are referred to the TBL unit. Diagnosis of TB was based on finding at least 2 out of the three samples positive for acid fast bacilli by Ziehl Neelson stain. Patients who are sputum smear negative but suspected to have TB are further evaluated with a chest radiograph, mantoux skin reaction, erythrocyte sedimentation rate and clinical assessment. Patients are then categorised as new patients (smear positive or smear negative), treatment after default. relapse and treatment failure case according to the national tuberculosis and leprosy control treatment guidelines. All smear positive and very sick smear negative TB patients are commenced on short course chemotherapy with daily rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months of intensive treatment followed by ethambutol/thiacetazone and isoniazid on outpatient basis for 6 months. Patients on re-treatment regime receive a 3 months intensive phase with the addition of streptomycin to the four drugs in the intensive phase mentioned above. The continuation phase is last 5 months with rifampicin, isoniazid and ethambutol three times a week. All patients routinely had pre and post test counselling for HIV screening using two methods namely the immunocombs II HIV 1&2 Bispot test kit (Orgenics, France) and the Capillus HIV-1/HIV-2 kit(Cambridge diagnostics, Ireland). A positive test is considered only when the blood sample is positive for the two test kits.

STUDY DESIGN

The study is a retrospective study of patients attending the tuberculosis and leprosy control unit of the Olabisi Onabanjo university teaching hospital Sagamu, between January 1997 to December 2003.All the patients admitted into the DOTS programme who were subsequently traced home and confirmed dead by relatives, family members and co-patients or patients under going treatment at the TBL unit who were admitted and died at the medical ward of the Olabisi Onabanjo university teaching hospital were regarded as 'dead'. Patients who died during treatment were matched for age and sex with those who completed their T.B treatment during the same period ('Alive') on the ratio 1:2. Patients on antiretroviral drugs during anti-tuberculosis treatment were excluded from the study.

DATA ANALYSIS

Data entry was done with Epi-info 6.04 statistical software. The dependent variable in the analysis was whether patient died or was alive at the end of eight months of anti-tuberculous treatment. A variety of independent variables such as HIV status of patient, sex, age, body weight at presentation, previous treatment of tuberculosis, sputum smear result were selected for potential inclusion in the model to discriminate between the outcome of dead or alive after treatment. Descriptive statistics were generated

for each variable; bivariate analysis were then conducted between each independent variable and outcome of treatment (i.e. whether Dead or Alive), using 2 independent sample t test andX2 analysis for continuous and discrete variables respectively. Variables that were statistically significant (P< 0.05) in the bivariate analyses were entered into a multiple logistic regression. Meaningful 2 way interaction effects between significant independent variables were investigated using contingency table analyses. The level of statistical significant in bivariate and multivariate analyses was taken at P≤0.05 Data was analysed using EPI 2002. The level of significance was set at p≤0.05 at 95% confidence limit.

RESULTS

A total of 946 patients were admitted into the TBL programme between January 1 1997 and December 31 2003 with a yearly average of 135 patients. A male: female ratio of 1:1 was observed in the study. A total of 53 deaths occurred during the study period giving a case fatality rate of 5.6%. Thirty one males and 22 females died with a ratio of 1.4:1 deaths. The death rates were lowest in 2002 and highest in 2003. The increase in the rate of death with tuberculosis rose from 5.4% in 1997 to 8.6% in 2003,an increase of 59.3%(Table 1).

The case fatality rates increased progressively from 3.9% in the 20-29year age group to 12.2% in the 50-59year age group. Higher mortality was seen in older patients from 50 years and aboce (Table II)

Table III. summarises the factors associated with dying during tuberculosis treatment in the study population. Those patients who died were significantly more likely to be HIV sero positive (p≤0.05) and to have had a previous TB treatment (p≤0.05). Other factors such as sputum smear acid fast bacilli negative result and preadmission weight were not significantly associated with mortality during TB treatment. About 60% of deaths during TB treatment was in the first two months. The interval between commencing treatment and dying was not significantly associated with HIV status (Table I II).In the multivariate analysis HIV remained the only predictor of death in the study population (OR 6.53 95% CI 2.80-15.3' P=0.00001) as shown in Table V.

Figure I shows the trend of both the annual HIV prevalence and mortality rates among TB patients during the study period.

TABLE I: YEARLY ADMISSION AND DEATHS AND ANNUAL DEATH RATES

YEAR	NO OF PATIENTS REGISTERED			NO OF DEATHS			ANNUAL DEATH RATE		
	M	F	TOTAL	M	F	TOTAL	M	F	TOTAL
1997	63	66	129	5	2	7	7.9	3.0	5.4
1998	64	65	129	4	3	7	6.3	4.6	5.4
1999	53	44	97	5	1	6	9.4	2.3	6.2
2000	65	81	146	3	6	9	4.6	7.4	6.2
2001	75	79	154	5	2	7	6.7	2.6	4.6
2002	82	58	140	3	1	5	3.7	1.7	3.6
2003	72	79	151	6	7	13	8.3	8.7	8.6
TOTAL	474	472	946	31	22	53	6.5	4.7	5.6
M:F RATIO	1:1			1.41:1			1.41:1		

TABLE II: ADMISSION, DEATHS AND FATALITY RATES BY AGE AND SEX

AGE (YEARS)	NO OF REGISTERED PATIENTS			NO OF DEATHS			FATALITY RATES		
	M	F	TOTAL	M	F	TOTAL	M	F	TOTAL
≤20	92	93	185	5	3	8	5.4	3.2	4.3
20-29	163	192	355	8	6	14	4.9	3.1	3.9
30-39	102	100	202	5	7	12	4.9	7.0	5.9
40-49	52	39	91	5	1	6	9.6	2.6	6.6
50-59	25	16	41	3	2	5	12	12.5	12.2
≥60	42	30	72	5	3	8	11.9	10.0	11.1
TOTAL	476	470	946	31	22	53	6.5	4.7	5.6

TABLE III: INTERVAL BETWEEN ADMISSION INTO THE TBL DOTS PROGRAM AND DEATH

TOTAL INTERVAL	HIV POSITIVE N=21	HIV NEGATIVE N=32	TOTAL (%)	CUMULATIVE FREQUENCY (%)
0-4 WEEKS	4	13	17(32.1)	17(32.1)
5-8 WEEKS	7	8	15(28.3)	32(60.4)
9-12 WEEKS	1	1	2(3.8)	34(64.2)
≥12 WEEKS	9	10	19(35.8)	53(100)
TOTAL	21	32	53(100)	

$X^2 = 2.72$

P =0.44

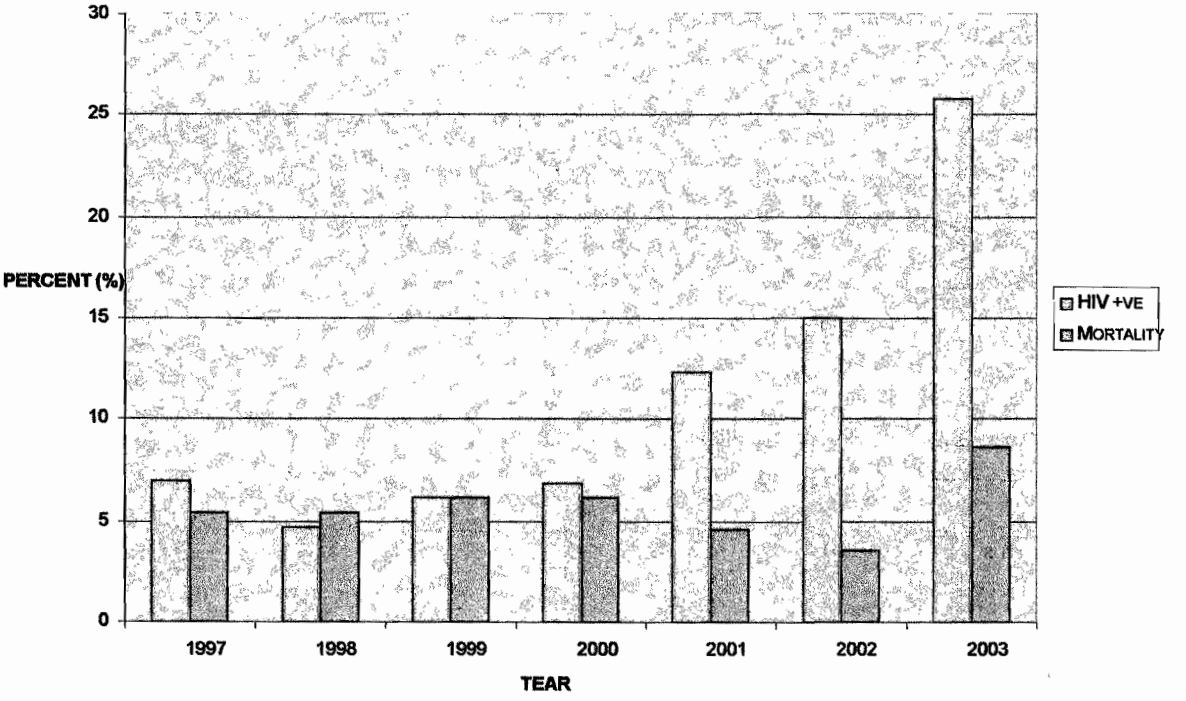
ABLE IV: FACTORS ASSOCIATED WITH DEATH DURING TB TREATMENT

FACTORS	DEAD N=53	ALIVE N=106	ODDS RATIO (C.I)	P VALUE
HIV POSITIVE STATUS	22(41.5)	10(9.4)	2.71 (1.84-3.79)	0.0001
SPUTUM SMEAR NEGATIVE	17 (32.1)	23(21.6)	1.70 (0.76-3.80)	0.12
PREVIOUS TB TREATMENT	10(18.9)	6(5.9)	3.88 (1.20-12.94)	0.009
PRE-ADMISSION WEIGHT	46.4±13.1	48.7±14.8	-	0.34

TABLE V: FACTORS ASSOCIATED WITH DEATH DURING TB TREATMENT

FACTORS	ODDS RATIO (C.I)	P VALUE
HIV POSITIVE STATUS	6.46 (2.7-15.3)	0.0001
SPUTUM SMEAR NEGATIVE	2.08 (0.89-4.87)	0.09
PREVIOUS TB TREATMENT	1.40 (0.44-4.5)	0.5
SEX	0.98 (0.47-2.1)	0.9

FIGURE I: HIV PREVALENCE AND MORTALITY RATES AMONG TB PATIENTS IN SAGAMU 1997-2003



DISCUSSION

The case fatality rate in this study was 5.6%. This is similar to an earlier study in the eastern part of Nigeria, which recorded an overall case fatality rate of 5.8%[9], but in contrast to 33% and 40% respectively in studies in Malawi[10,11] .The high death rate among tuberculosis patients in the later studies may be related to the high HIV prevalence rate of 84-89% among TB patients in the above mentioned countries.

Case fatality rate in this study was observed to increase with age. Although death rate was highest in the 50-59 year age group, 75% of the total deaths still occurred in individuals less than 50 years. This is in contrast to earlier studies in the developed countries where more deaths occurred in individuals who are 65 years and above[12] . This underscores the difference in the epidemiology of TB in developed countries compared to developing countries. People in developing counties are exposed to TB earlier in life and so die younger due to several factors including inadequate and inaccessible diagnostic and treatment facilities, overcrowding, and poverty[13]. However, recent studies in many developed countries show a new peak spanning the ages 20-49 years accompanying the pre-existing peak in the elderly[14]. The AIDS epidemic has been observed to be responsible for the significant increase in the number and rate of tuberculosis death in younger adults[15].

HIV co-infection was associated with increasing mortality in this study. The annual case fatality rate rose from 5.4% in 1997 to 8.6% in 2003, an increase of 59.3%.These observation have also been reported in similar studies[4].

Another factor associated with mortality was history of previous treatment of TB. Patients previously treated who did not comply strictly with their medications are at risk of developing multi-drug resistant strains that are difficult to cure with the current anti-TB regimen in the DOTS programme and this may contribute to mortality in these patients.. Other factors such as sputum smear negativity for acid

fast bacilli and pre-admission weight were not significantly associated with mortality in our study. Other studies however observed that smear negative AFB was significantly associated with mortality[10,11]. HIV infection has been associated with atypical presentation such as sputum smear negative result or extra pulmonary TB which may lead to diagnostic delay thereby contributing to mortality[17]. The mortality in smear negative patients may however be due to diseases other than TB. The time interval between commencement of TB treatment and death was not related to HIV status. Other studies however reported that non HIV infected patients died early in treatment compared with TB/HIV positive patients[10,11] .The interval between diagnosis and death in the present study was much longer compared with other studies. This may be as a result of late presentation in studies done among medical in patients[9,18]

The factors contributing to death could not be ascertained in this study. as most of the patients died at home being unable to afford hospital admission. This is in keeping with earlier observation that majority TB deaths takes place outside the hospital settings[19].

In conclusion the present study which analysed deaths from tuberculosis in patients attending an out patient TBL control centre *in* Sagamu observed an upward trend in mortality and also found HIV infection to be the only predictor of death in multivariate analysis.

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