

MORTALITY AMONG TUBERCULOSIS PATIENTS AT THE EFFIA-NKWANTA REGIONAL HOSPITAL: 1999-2001

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SUMMARY

The study was undertaken to examine factors associated with death among all TB patients registered for treatment in 1999-2001.

A database for registered TB patients was sorted into six treatment outcomes. Five outcomes (except death) were combined into one variable named "survivors" and compared with those who died. Time analysis of death was performed using Kaplan-Meier's survival method.

Case Fatality Rate (CFR) for all forms of TB was 13.3%. The CFR was significantly higher among patients above 45 years ($p=0.001$), smear negative ($p=0.001$), pulmonary TB ($p=0.02$) and HIV positive patients ($p=0.001$). The CFR was higher among males and patients put on the Re-treatment regimen but the differences were not statistically significant when compared to survivors ($p=0.125$ and 0.07 respectively). The mean time of death was 3 months. The overall probability of a patient surviving the second and sixth month after starting treatment was 42.3% and 5.2% respectively.

Mechanisms to reduce the number of patients put on the re-treatment regimen should be established. Further studies are needed to establish the cause of the higher CFR observed among males and smear negative patients.

Keywords: Tuberculosis; Case Fatality Rate, Mortality, Effia-Nkwanta Regional Hospital

INTRODUCTION

Globally, more than 8 million cases of tuberculosis (TB) are notified each year, of which 2 million prove fatal, thus making TB the world's largest single infectious cause of death in spite of the widespread availability of highly effective drugs¹. The burden of the disease is mostly felt in developing countries, notably sub-Saharan Africa, where the HIV/AIDS epidemic is the single most important factor responsible for the observed increase².

Because of the increasing global incidence of the disease, the World Health Organization (WHO) declared tuberculosis a global emergency in 1993 and set a target of detecting 70% of new infectious cases and cure 85% of those detected¹. In order to achieve cure for 85% of detected cases, there is the need to look at indicators that will influence the attainment of this target.

Mortality from TB is one of such key TB control programme performance indicators and is also likely to be a significant factor affecting control programme credibility in the affected communities. The survival of patients with TB depends on several factors, including age, socio-economic status, co-existing disease, condition on presentation for treatment and quality of treatment provided³.

The objective of this study was to retrospectively examine factors associated with mortality among TB patients registered for treatment between January 1999 and December 2001 at the Effia-Nkwanta Regional Hospital (ENRH) and to make recommendations if any, to improve management of TB cases at the hospital.

SUBJECTS AND METHOD

Study setting

This study took place at the ENRH which is located in the Shama Ahanta East Metropolitan district of the Western Region of Ghana. The ENRH has a Unit called the Communicable Diseases Unit (CDU) where all TB patients receive treatment. The CDU is a 54-bed capacity facility that provides treatment for TB patients from the surrounding towns and villages. It also serves as the referral unit for complicated cases of TB seen in other hospitals within the region.

TB diagnosis and treatment at the ENRH

Cases of TB are diagnosed among patients reporting to the Out-Patient Department (OPD) of the hospital. Individuals who presented with cough

lasting for three weeks or more are made to undergo sputum smear microscopy and chest x-ray examinations. Those found to be suffering from TB are then referred to the CDU where they are registered and started on TB treatment.

During the intensive phase of treatment, most TB patients are supplied with their drugs and then transferred to a health facility nearer to their normal place of residence to receive treatment. Patients living near the CDU come there every morning for treatment. About 90% of patients are managed on this ambulatory basis for the entire intensive phase. However, patients who are severely ill or have other medical complications that will not permit ambulatory treatment are admitted to the CDU for treatment.

During the continuation phase, all patients are seen at the CDU every month on ambulatory basis irrespective of where treatment was received during the intensive phase. This enables review of progress of treatment to be made as well as the supply of medications for the proceeding month.

The treatment regimens used at the CDU are those recommended by the WHO and used by the National Tuberculosis Control Program (NTP) throughout the country⁴. Briefly, three treatment regimens are used, namely Re-treatment (RTR), Short Course (SC), and Standard Treatment (ST). The RTR regimen (2SRHZE/1RHZE/5R₃H₃E₃)* is used for patients with previous history of TB treatment such as relapse, treatment failure and treatment after default. The SC regimen (2SHRZ/6HT) is used for new sputum smear positive and severely ill smear negative and extra-pulmonary patients. The ST regimen (2SHT/10HT) is used for smear negative and extra-pulmonary patients.

HIV testing

There is no firm HIV testing policy for TB patients registered at the CDU. However, since 1998, records are kept of patients whose HIV status is known. The establishment of the HIV status is done in three ways.

- Most of the TB patients registered for treatment at the CDU come with HIV results re-

quested by health staffs in other departments of the hospital where they first reported to when their sickness started.

- The second way of establishing the HIV status is during TB treatment. Patients who react to the anti-tuberculosis drugs, especially thiacetazone are made to under go voluntary counselling and testing for HIV infection.
- If there are other reasons, for instance, signs and symptoms to suggest HIV infection whilst the patient is on TB treatment, HIV screening can be requested by the medical team attending to the patient.

Based on this "HIV status register", patients were classified as HIV-positive, HIV-negative and HIV unknown.

Data collection technique and analysis

Using the Institutional TB register from 1999 to 2001 an SPSS database was created for all TB patients registered at the CDU. The data was then sorted into six treatment outcomes- cured; treatment completed; defaulted; died; treatment failure and transferred out. Five outcomes (except died) were combined into one variable and named "survivors". Those patient named survivors were then compared with those who died in other to identify factors associated with mortality at the hospital. Patients with no declared outcome in the register were excluded from the analysis.

In order to obtain detailed records on stage of treatment when death occurred, the medical records of those who died were retrieved and the duration of treatment received before death was extracted. Time analysis of when treatment commenced until death was performed using Kaplan-Meier's survival method. Statistical analysis of the whole data was performed using SPSS 10.1 for Windows. For the analysis of factors associated with mortality, p-values were calculated by univariate and multiple linear regression analyses. Statistical significance was taken as $p < 0.05$.

RESULTS

A total of 1599 cases of all forms of TB were registered for treatment during the three (3) years under review, 114 (7.1%) of them had no outcome declared in the register and were therefore excluded from the analysis. Out of the 1485 patients with declared outcomes, 446 (30%) were cured, 503 (40%) were treatment completers, 226 (15.2%) were defaulters, 55 (3.7%) were treatment failure, 57 (3.8%) were transferred out and 198 (13.3%) died. Medical records for the determina-

* R= Rifampicin; H= Isoniazid; Z = Pyrazinamide; E = Ethambutol; S = Streptomycin. Numbers before the letters indicate the number in months of the phase of treatment; numbers in subscript indicate the number of times the drugs are taken each week.

tion of time treatment commenced until death was available for 191 of the 198 (96.5%) who died during treatment.

The Case Fatality Rate (CFR) for all forms of TB for the 3-year period under review was 13.3 %. The mean and modal ages for the dead were 47 and 50 years respectively. The corresponding ages

to the survivors ($p= 0.001, 0.001, 0.001$ and 0.02 respectively). The male gender and patients put on the RTR regimen also had higher CFR, but the differences were not statistically significant when compared to the survivors $p=0.125$ and $p=0.070$, respectively. Factors associated with mortality among the patients are shown in Table 1.

Table 1 Factors associated with mortality among patients with tuberculosis at ENRH, 1999-2001

Variable	No of Survivors	No of Deaths	Case fatality		P-value	
			Total	Rate (%)	Univariate	Multivariate
All patients	1287	198	1485	13.3	0.001	-
Gender						
Male	783	140	923	15.2	-	-
Female	504	58	562	10.3	0.008	0.125
Age (years)						
0-24	319	15	334	4.5	-	-
25-44	604	74	678	10.9	-	-
45+	364	109	473	23.0	0.001	0.001
Sputum Smear Type						
Smear positive	774	88	862	10.2	-	-
Smear negative	403	93	496	18.8	-	-
Unknown*	110	17	127	13.4	0.001	0.01
Treatment Regimen						
Short course	1163	179	1342	13.3	-	-
Re-treatment	89	17	106	16.0	-	-
Standard treatment	35	2	37	5.4	0.261	0.070
Type of TB†						
Pulmonary	1261	198	1485	13.6	-	-
Extra-pulmonary	26	0	26	0	0.044	0.020
HIV Status‡						
Positive	49	45	94	47.9	-	-
Negative	68	11	79	13.9	-	-
Unknown	1170	142	1312	10.8	0.001	0.001

*Sputum smears were either not done or needed for 110 patients (extra-pulmonary and paediatric cases)

†TB-tuberculosis

‡HIV status was unknown for 1312 survivors

for the survivors were 36 and 30 years respectively.

CFR was highest among patients above 45 years of age, smear negative type of TB, HIV positive status and pulmonary TB patients; and the differences were statistically significant when compared

One hundred and one (101) deaths (52.9%) occurred during the intensive phase of treatment; compared to 77 deaths (40.3%) during the continuation phase. Thirteen deaths (6.8%) occurred before treatment could be started.

Kaplan-Meier survival analysis of time treatment started until death (Figure 1) showed that the mean time of death was 3 months and the probability of a patient surviving second and sixth month after starting treatment was 42.3% and 5.2% respectively.

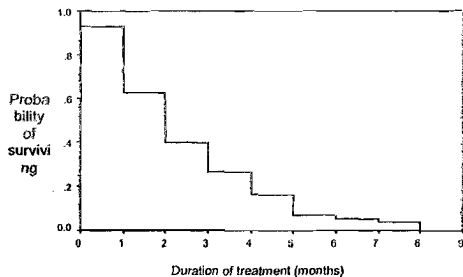


Figure 1 Kaplan-Meier survival curve for patients who died from TB (99-01)

DISCUSSION

The limitations of this study include the fact that the data used is hospital based and therefore patients who died at home may not be included in the hospital records leading to under-estimation of the death rate. Furthermore, the inclusion in the analysis of defaulters (some of whom may have died at home and may be "mis-classified" as defaulters) and patients transferred out to other treatment centres for which no treatment outcomes have been sent to the CDU may affect the mortality rates. The exclusion of 114 records with no outcome data in the register may also affect the mortality rate calculated.

The CFR of 13.3% in this study is comparable to results from other developing countries like South Africa (13%)⁵ and Santa Cruz, Bolivia (15.7%)⁶ but is far higher than 0.5-4.5% obtained in most developed countries⁷. However, in other developing countries where there is higher proportion of dual infection of TB/HIV, for instance 85% in Zimbabwe⁸, the mortality rate was found to be 21%.

The higher CFR among males compared to females has been observed in Lithuania⁹ and Yugoslavia¹⁰, where death among males was 6.4 and 3 times more compared to females respectively. Although preponderance of males among TB patients is well documented in Ghana⁴, the fact that employment opportunities in and around Shama Ahanta East Metropolitan District (where ENRH is located) is mainly male dominated with its associ-

ated risks, might have accounted for the difference in mortality pattern seen in this study¹¹.

Although the unavailability of data on the prevalence of other chest related diseases as well as the age-specific mortality rate of the background local population may affect the mortality rate reported in this study, the results indicate that those above 45 years are at higher risk of death from TB compared to younger patients. The higher CFR among this age group may be attributed to decrease in immune status with age, the burden of other infectious and respiratory diseases; this observation should however, be investigated further.

The significantly higher CFR among smear negative patients compared to smear positive patients coupled with the fact that 61% of the smear negative deaths occurred during the intensive phase of treatment have been observed elsewhere⁴. This observation may be attributed to the difficulty of accurately diagnosing smear-negative TB in most resource poor countries including Ghana. The unavailability of sputum culture for diagnostic purposes in Ghana, for instance could lead to the situation where some of the patients might be suffering from other respiratory diseases but may be misdiagnosed as smear negative TB. This finding warrants further studies to establish the cause of death in this group of TB patients.

The slightly higher CFR found among patients put on the RTR regimen may be due to prolonged duration of TB disease coupled with the risk of Multiple Drug Resistant TB (MDR-TB) in such category of patients. This is because patients put on this treatment regimen have previously received TB treatment for various durations. The combined effect of these risk factors could result in the higher CFR observed.

The proportion of dual infection of TB/HIV is not known in Ghana, but a study conducted by Frimpong et al among hospitalised TB patients in Kumasi put the prevalence rate at 23.2%¹². The higher CFR found among HIV positive patients in this study must be applied with some caution since the HIV status of a large proportion (88.4%) of the patients was not known. However, recognising that the group of patients with unknown HIV status represents a mix of HIV-infected and non-infected patients, certain broad conclusions can be drawn from the results of this study.

What is the cause of the early mortality (Figure 1) observed in this study? Although no autopsies

were done to ascertain the cause of death, the high mortality rate may be attributed to delay in seeking treatment on the part of patients and diagnostic delay on the part of health care providers. This problem of patient and doctor delay in diagnosing TB has been studied by Lawn et al in Ghana⁸. They found that the median doctor delay from the first consultation until diagnosis was double the median patient delay at initial presentation (8 weeks versus 4 weeks).

Another factor that may affect early death is the timeliness of supply of drugs and other logistics needed for TB control activities. Key Informant Interviews conducted at the CDU revealed that there were temporal shortages of drugs at certain times of the periods under review. This led to the situation where patients had to wait for weeks before starting treatment resulting in death of some of the patients before treatment was started.

The other cause of the high case fatality among TB patients is due to the HIV/AIDS menace which has engulfed sub-Saharan Africa and was highlighted by other studies^{2, 3, 5, 8}.

CONCLUSION

This study has demonstrated some of the factors that may affect CFR among TB patients. The ENRH should put in place mechanisms to reduce the number of patients put on the RTR regimen, especially minimising defaulter rate, since the risk of development of MDR-TB is high in such patients, leading to high CFR.

Periodic refresher training programs should be organised for staff of the hospital in order to improve timely diagnosis and early treatment of patients. Drugs and other logistics needed for TB control should be supplied on time so that appropriate treatment and care can be instituted for patients.

Although further studies are needed to establish the cause of the higher CFR observed among males and smear negative patients, the establishment of Voluntary Counselling and Testing (VCT) for HIV infection in TB patients could make prophylaxis with Co-trimoxazole which is known to reduce mortality among HIV infected TB patients possible.¹³

Until efforts are made to find out the causes of the high CFR among TB patients registered for treatment and corrective measures instituted if possible, the Western Region and Ghana as a nation

will not be able to achieve the target of successfully treating 85% of smear positive cases set by the WHO.

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