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RESEARCH ARTICLE

SURVIVAL ANALYSIS OF AVERAGE RECOVERY TIME OF TUBERCULOSIS PATIENTS IN NORTHERN REGION, GHANA

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ABSTRACT

In this study, the average recovery time of Tuberculosis patients and the associated risk of treatment failure were examined based on a retrospective moving cohort of sixty-one patients in Northern Region, Ghana. Cox regression was used for multivariate analysis whiles Product-Limit estimator was used to estimate the average recovery time of tuberculosis patients. It was observed that the survival rates for males and females were 85.71% and 88.46% respectively. It was discovered that, age of patient at diagnosis, category, and type of patient were crucial determinants of treatment outcome. The study reported a median recovery time of 22 weeks in the Region. The risk of relapse and death were found to be related to age. It was also realized from the study that most of the deaths occurred within the first three weeks of treatment. Although, it is generally reported that the levels of drug resistance in Africa are lower than in other parts of the world, measures to provide controlled application of second-line drugs, supervision of drug distribution and compliance, enforcement of Directly Observed Therapy–Short course protocols, and sustained training of all personnel involved in tuberculosis management should be enforced for effective combat of the tuberculosis disease.

INTRODUCTION

Tuberculosis is a common and often deadly infectious disease caused majorly by *Mycobacterium tuberculosis* in humans (Kumar, Abbas, Fausto & Mitchell, 2007). It was first isolated in 1882 by Robert Koch, a German physician who received a Nobel Prize for his discovery. Tuberculosis attacks the lungs but can also affect other parts of the body. It is an air borne disease which spread through coughing, sneezing, and spitting by infected persons (Konstatinos, 2010). Many researches on tuberculosis (TB) treatment have reported varying recovery times. Gavrilenko (2001) reported that if TB is detected early, it can be treated in six months whiles it takes between six to ten years to treat for late detection. Addition of the antibiotic moxifloxacin to the usual TB drugs reduces recovery time from six to four months (Alice, Janet & Henry, 2001). It is estimated that Ghana has 123 smear positive pulmonary TB cases per 100,000 population and 281 of all types of TB cases per 100,000 population per year. This means that, Ghana with a population of about 20 million should expect about 25,000 smear positive pulmonary TB cases and 56,000 new TB cases of all types every year with about 12,000 deaths (NTP Report, 2006). The incidence of TB cases for the years, 2007, 2008 and 2009 in Northern Region were 545, 677, and 556 respectively. With this observation, much attention need be paid to the incidence of TB, which therefore informs the need for this research study. The main objective of this research is to model the average recovery time of tuberculosis patients in Northern Region, Ghana using a survival function.

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MATERIALS AND METHODS

The research considered tuberculosis cases from the entire Northern Region of Ghana because patients were admitted from all over the Northern region and detained for treatment at the Baptist Medical Center, Nalerigu and Tamale Teaching Hospital where the data used for this study were obtained. The data consist of a retrospective moving cohort of 61 patients enrolled at the centres between January and April, 2010. For the sake of this study, a patient was considered cured, if and only if he/she is negative to Smear+ Test. The time of treatment was determined by calculating the difference between time of initiation and outcome of treatment. The prognostic factors in the data include: age, sex, date treatment started, date treatment completed, disease classification, category of patient, outcome of treatment, and type of patient. The study did not have direct patient involvement, therefore, ethical clearance was not needed. The 61 patients were observed over seven months. Patients who die, or got treatment failure, or whose recovery time exceeded the seven months in the course of the treatment were considered censored. The product-limit function (2.1) was used to study the survival pattern of the patients in which the survival probability after each week of treatment initiation was studied. The group variables studied included category of patient and sex. The product-limit function is defined by

$$\hat{S}(t) = \prod_{j:t_j \le t} \left[1 - \frac{d_j}{n_j}\right] \text{ for } t_1 \le t \le t_k \quad \ldots\ldots(2.1)$$

The Cox Proportional Hazards Model (2.2) was used for multivariate analysis of the various prognostic factors studied The Cox proportional model is given by

$$h_i(t) = \lambda_o \exp\{\beta_1 X_{i1} + ... + \beta_k X_{ik}\} \quad (2.2)$$

$$\lambda(t) = \lim_{\Delta t \to 0}\left[\frac{pr\{t < T < t + \Delta t \mid T \geq t\}}{\Delta t}\right] \quad (2.3)$$

$$\lambda(t) = \lim_{\Delta t \to 0}\left[\frac{pr\{t < T < t + \Delta t \mid T \geq t\}}{\Delta t}\right] \quad (2.4)$$

The hazard function describes the concept of the risk of an outcome (e.g., death, failure, hospitalization) in an interval after time t, conditional on the subject having survived to time t. It is mathematically defined as; The validation method employed in the study was the Jacknife technique for average recovery time.

RESULTS

The study was conducted on a retrospective moving cohort of sixty-one TB patients admitted into Directly Observed Therapy-Short course (DOTS) programme in the Northern Region of Ghana. Of the sixty-one patients studied over the specified period, 35 representing 57.38% were males and 26 representing 42.62% of the patient population used were females. Patients who were diagnosed with TB for the first time was 88.52% with 11.48% relapse cases. The percentage of patients in Categories I, II, and III were 73.77%, 13.11%, and 13.11% respectively. About sixty-six (65.57) percent of the patients had Pulmonary TB, while 34.43% were diagnosed with extra Pulmonary TB. About Sixty-nine percent of the patients recovered with thirty-one percent treatment failure.

Estimation of Average Recovery Time using the Product-Limit Method

The product–limit method was employed in estimating the average time to recovery of TB patients in the Northern Region. The probability of recovery in 10 weeks was 0.9836 and the estimated probability of death prior to 10 weeks was 0.0164. The 50th percentile, which is the median recovery time, was 22 weeks.

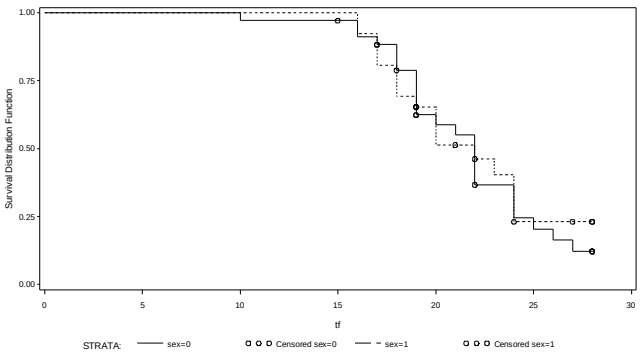

Fig. 1. Survivor Functions for Males and Females

The 25th percentile was 18weeks which is the smallest recovery time such that the probability of dying is 0.25 The mean recovery time was determined to be 21.5786 with a standard error of 0.5315, but due to the fact that the largest event time was censored, the mean and its standard error were underestimated and hence biased. Using the Jackknife technique, an average recovery time of 20.4918 with a standard error of $6.7592*10^{-31}$ was obtained which well approximates

Table 1. Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr>Chisq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Sex	1	0.1623	0.32748	0.246	0.6202	1.176	0.595	2.156
Age	1	-0.0461	0.01174	15.41	<0.0001	0.955	0.936	0.980
Dcv	1	-0.3518	0.39235	0.804	0.3699	0.703	0.329	1.526
Cv	1	1.69306	0.36199	21.87	<0.0001	0.226	0.071	0.887
Tpv	1	-1.4856	0.64029	5.383	0.0203	5.436	2.485	10.321

LEGEND: Dcv – Disease Classification of patient, Tpv – Type of patient
Cv – Category of patient, Age – Age of patient at the time of admission into the study
Sex – Whether the patient is male or female, DF - Degrees of freedom.

the result of the product-limit estimator. Hence the product-limit estimator provided a good estimate of the median recovery time of 22weeks. Controlling for sex, the Wilcoxon statistic (0.0056, Pr=0.9405) showed that there was no significant difference in recovery times for both sexes. The plot of the survivor function for this is presented in Fig. 1. From Fig. 1, it could be observed that the two survivor curves were the same until the 10th week when the curve for the males started a gradual fall. The curves are indistinguishable and serve as a confirmation of the earlier result that there was no statistically significant difference in recovery times between males and females. However, there were differences in average recovery times among categories I, II, and III with a Wilcoxon statistic of 12.7957 and Pr=0.0017.

Cox's Proportional Hazards Model

The Cox's Proportional Hazard Model was employed to determine the hazard ratio of the various covariates. The result obtained by the PHreg procedure is shown in Table 1. Clearly, the variables whose effect on time to recovery significantly differs from 0 include age, category of patient (Cv), and type of patient (Tpv) respectively. The highest hazard ratio was associated with category of patient while the minimum falls to type of patient. The Likelihood Ratio test showed that at least one of the covariates are significantly different from 0 (Table 1).

DISCUSSION

A larger percentage of the patients in this study were males with 68.57% of the diagnosis being pulmonary positive but fell short of the results of another study (NTP Report, 2006), which stated about 80% of pulmonary positive cases in Ghana. The median recovery time of 22weeks (approximately 6months) obtained in this study was significantly less than the estimated time of 9 months reported by WHO. The results of the Jackknife technique proved that the estimate was of remarkable precision as both estimates were as close as possible. Perhaps further investigations could even help shortened the time as reported by other researchers (Gavrilenko, 2001, Alice, Janet & Henry, 1909). It has been reported that, among the deaths in TB patients, the median time from treatment initiation to death is 35 days (Dewan et al., 2004). Fox, et al. (1999) had reported that clinical relapse occur after three to six months of treatment. This interval is the same as 12weeks to 24weeks as experienced in this study.

The success rate for females in this study was 65.38%, while that of males was 71.43%. Although this seem encouraging, it however, fell short of WHO's target of 85% according to NTP (2006). The survival rates in this study were found to be 86.67%, 75.00% and 75.00% in categories I, II and III, whiles survival rates reported in another study in India (Pardeshi, 2009) are 93%, 88% and 96% in categories I, II and III, respectively. The survival rates for males and females were also found to be 85.71% and 88.46% respectively. However, Pardeshi (2009) reported death rates of 5.80% and 5.59% to males and females respectively. 'Age is an important risk factor for death in tuberculosis patients' (Pardeshi & Deshmukh, 2007), because most of the prolonged recovery periods and deaths were noted in the elderly. 'Apart from the increased physiological risk of death, the vague symptoms in the elderly, diagnostic problems and concomitant illness could be some of the contributing factors for the increased death rate in the elderly' (Pardeshi, 2009). Screening the patients for these diseases and managing them appropriately will therefore be important. Additionally, it was realized in this research that for each one-week increase in age after treatment initiation, the risk of treatment failure goes down by 6.4% holding all other factors constant. But this rate could be impeded by the aforementioned factors especially in the elderly. The negative signs of the coefficients of parameter estimates indicate that they are associated with a reduction in recovery time. But they are less informative (Paul, 2009) than the p-values which are commonly used for interpretation. Because secondary data was utilized for this study, a number of other factors such as addictions, co-morbidities, dietary system, pre-treatment weight, HIV status could not be studied.

The constant graph of the survivor function (Fig. 1) for both males and females in the first 10weeks attest to the fact that no recovery is possible within that period. There after, the graph for the males declined between 10 and 15 weeks, indicating that some of the patients had recovered. The females however, started their recovery after 15weeks. This observation probably serves as a manifestation of the fact that patients are kept on strong antibiotics (NTP, 2006) during the intensive phase of treatment to avoid the bacteria developing resistance against these drugs, therefore, the risk of treatment failure is minimize, hence maintaining the balance which gave the constant graph. Although this study showed that, the risk for death (treatment failure) in female patients was 17.6% higher than that of males, the p-value did not show any significant difference in recovery times between males and females holding the effects of other factors constant. Ponnuraja and Venkatesan (2010) however reported in their study that males seem to have significantly larger response time than females. Patients who are diagnosed with TB for the first time (new TB diagnosis) had 22.6% risk of treatment failure as compared to patients who have relapse cases holding all other factors constant. This supported the statement by NTP (2006) that treatment failure is more difficult to diagnose and treat, hence the high failure rates. Patients diagnosed with extra pulmonary TB have 5.436 times risk of treatment failure as compared to those with pulmonary TB holding the effect of all covariates constant. This may be due to the fact that extra pulmonary TB is generally difficult to diagnose (CDC, 2000). It needs an experience doctor to confirm and at times involve the use of an X-rays imaging or scans, and tuberculin skin test among others (Konstantinos, 2010). It will therefore be important that greater care is taken when dealing with the elderly. Health personnel should also reach out to the rural communities as this will promote early detection.

REFERENCES

Alice A. J., Janet M. H. & Henry H., M. L. 1909. *Household Companion: The family Doctor*. Dewsnap.

Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination. Core Curriculum on Tuberculosis: What the Clinician Should Know. 4th edition (2000). Updated August 2003.

Dewan, P. K. Arguin, P. M. Kiryanova, H. Kondroshova, N. V. Khorosheva, T. M. Laserson, K. Kluge, H. Jakubowiak, W. Wells, C. Kazionny, B. 2004. Risk factors for death during tuberculosis treatment in Orel, Russia *Int J Tuberc Lung Dis*, , 8(5):598–602 © 2004 IUATLD

Fox W, Ellard, G. A and Mitchison D. A. 1999. Studies on the treatment of tuberculosis undertaken by the British Medical Research Council tuberculosis units, 1946-1986, with relevant subsequent publications. *Int. J. Tuberc. Lung. Dis*. 3:231-79.

Gavrilenko, V. S. 2001. *Recovery criteria and time in patients with pulmonary tuberculosis*. Tuberk, (8): 10-4.

Konstantinos, A. 2010. "Testing for tuberculosis". *Australian Prescriber*, 33:12-18. http://www. Australi anpres criber. com/magazine/33/1/12/18/

Kumar, V., Abbas, A.K., Fausto, N. and Mitchell, R. N. 2007. *Robbins Basic Pathology* (8thed.). Saunders Elsevier. pp. 516–522.ISBN 978-1-4160-2973-1.Manual, introduction to DOTS (TB) Programme, NTP Ghana, 2006.

Pardeshi G, & Deshmukh D. 2007. Disease characteristics and treatment outcome in elderly tuberculosis patients on DOTS. *Indian J Community Med*, 32:292-4

Paul D. A. 2009. *Survival Analysis Using SAS; A practical Guide*, SAS Institute Inc.

Ponnuraja C. and Venkatesan P. 2010. Survival models for exploring tuberculosis clinical trial data-an empirical comparison, *Indian Journal of Science and Technology*, ISSN: 0974- 6846, Vol. 3 No. 7 pp 755-758

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