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Estimation of the expected period of acquired tuberculosis to become a chronic tuberculosis

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Abstract: In order to assess hazards pose by chronic tuberculosis, a table similar to a life table is prepared to estimate the expected period of the acquired tuberculosis to become chronic tuberculosis. This is ailment attributable to the Mycobacterium tuberculosis. Confidence bounds for the estimate were also derived. An example is given using a data set from University of Ilorin Teaching Hospital, Ilorin in Kwara State, Nigeria where some tuberculosis patients were monitored over some years. The available data were analyzed using Statistical Package for Social Sciences (SPSS) version 15, Chicago Inc., IL, and USA. The results show that for the potential patient(s), the expected period of developing the Tuberculosis is 6.796 years before the infection become chronic infection (Tuberculosis). Therefore, 95% confidence interval for the estimated period was found to be between 6.7763 and 6.8157. Hence, it is recommended that health policy maker should formulate policies that curb the pandemic of the disease.

Keywords: Tuberculosis, Mycobacterium, Parameter, Life Table

1. Introduction

In statistics, while estimating parameter, it is obvious that such parameter is either arising from or assumed to be arising from a population (or a model). So, the expected period of acquired tuberculosis to become chronic tuberculosis is similar to life expectancy, which is a component of a life table. Tuberculosis (TB) is a chronic infectious disease caused by a bacterium called Mycobacterium tuberculosis. It is usually affect lungs in 80% of cases with warning signs of cough, haemoptysis, and chest pain, shortness of breath; fever, weight loss, and drenching night sweat [14, 17,18]. Tuberculosis is spread mainly through the air inform of droplets. When infectious people cough, sneeze, talk, laugh or spit, droplets containing Mycobacterium tuberculosis are sprayed into the air. People nearby may inhale the bacteria and become infected. Mycobacterium tuberculosis can remain viable as air-borne droplet suspended in the air for a long time or as part of house dust for weeks. However, transmission usually occurs only after substantial exposure to someone with active tuberculosis [14, 18]. A person can be infected by Mycobacterium tuberculosis for many years without getting sick or spreading the organism to other people. If the immune system is weakened by immunosuppressive disease like HIV infection, diabetes mellitus, malignancy, chronic kidney disease, extremes of ages, and immunosuppressive agent, latent tuberculosis infection can develop into active disease [1, 14, 18]. If a person with active disease is left untreated, he or she will infect on the average between 10 and 15 people every year [2, 3, 6]. Tuberculosis accounts for 2.5% of the global burden of disease and is the commonest cause of death in young women, killing more women than all causes of maternal mortality combined [1, 4, 5, 22]. Ninety-five per cent of all cases and 99% of deaths occur in developing countries, with the greatest burden in sub-Saharan Africa and South East Asia [3, 20]. It currently holds the seventh place in the global ranking of causes of death [1-5]. Unless intensive efforts are made; it is likely to maintain that position through to 2020, despite a substantial projected decline in disease burden from other infectious diseases [6, 13, 20]. Tuberculosis causes a significant socioeconomic burden: as three quarter of cases are within the economically productive age group of 15-54 years [17]. Tuberculosis is a serious public health problem in Nigeria with an estimated prevalence of nearly 900,000 tuberculosis cases and with the second highest tuberculosis disease burden in Africa and ranks 5th among

the 22 high tuberculosis burden countries in the world [5]. In Nigeria, there were 90,447 cases notified in 2010 with 41,416 (58%) cases as new smear positives, and a case detection rate of 40%. Ilorin city is the capital of Kwara State, a state that has one of the least Tuberculosis notification rates (900 per annum) when compared with other states in the country like Lagos (8200 per annum) and Oyo (6000 per annum) that have the higher tuberculosis notification rate [11,12,14]. The outcome of tuberculosis control is determined by the clinical and social factors like delayed presentation and health care utilization which depend on the knowledge and awareness of tuberculosis Symptoms among the population [4, 7, 14]. For us to meet the Millennium Development Goal (MDG), the Global Plan to Stop Tuberculosis and reverse the incidence of tuberculosis by 2015, we need to determine the level of awareness of the warning signs, risk factors, and treatment of tuberculosis among the population as modifiable factors in the tuberculosis control program [1, 2]. Tuberculosis continues to remain a significant threat even as we have moved into the second decade of the 21st century. As a matter of fact Tuberculosis has assumed an even more ominous stance with the emergence of totally drug resistant or TDR Mycobacterium tuberculosis strains which are virtually untreatable [4,19,20]. Unfortunately, there has been no new effective vaccine against tuberculosis, and in spite of introduction of several new drugs like bedaquiline, delamanid, PA824, or SQ109 and a new generation of fluoroquinolones like gatifloxacin and moxifloxacin, they are yet to be involved in the current routine antituberculosis regimen, though clinical trials for combinatorial therapy along with currently used drugs are underway [12, 21]. The emergence of resistance against these new classes of drugs is also a likely possibility which will result in the same problems in the future with newer group of drug-resistant strains, as we are facing today with the multidrug resistant (MDR) and extensively drug-resistant (XDR) strains [4,12,18,20]. Under these circumstances, rapid and definitive molecular diagnostics for effective intervention and treatment of Tuberculosis patients is a cornerstone for appropriate disease control and eradication [7]. Recently, a lot of attention has been devoted towards rapid Tuberculosis diagnostics especially those which enable rapid drug susceptibility testing (DST) to break free from the century long dependence on smear microscopy and culture methods, which are frustratingly insensitive and time consuming, respectively. WHO has recently recommended automated liquid culture systems, line probe assays, and the Xpert MTB/RIF tests which allow faster DST results and highly sensitive detection of Mycobacterium tuberculosis from clinical samples [7, 13, 14].

Tuberculosis represents a major public health concern especially due to the increasing number of multidrug-resistant tuberculosis TB (MDR TB). Particularly in developing countries, extensively drug-resistant tuberculosis TB (XDR TB) continues to pose serious problem [1–5]. The increase in MDR/XDR TB rates prompts effective diagnos-

tic methods so that appropriate treatments can be given to infected patients [6–8]. Many studies reported that MGIT 960 (Becton Dickinson Diagnostic System, Sparks, MD) provided reliable and rapid results in the detection and recovery of mycobacterium from clinical specimens and also the drug susceptibility testing (DST) of the TB isolates for the first line drugs isoniazid, rifampicin, ethambutol, streptomycin, and pyrazinamide [9, 10]. Recently, laboratories are facing great hindrances to provide DST for second-line drugs to ensure effective treatment of MDR/XDR TB by using MGIT 960 system [11–16]. However, in most of these studies, the tested numbers of second-line anti-TB drug were limited and the critical concentrations ranges of the second-line drugs were also discordant [11–13]. Despite the recommendation by WHO in 2008 for the use of liquid media for the second-line DST using MGIT 960, it is still unreliable due to the difficulty in determining the critical concentration [16]. It is not easy to calibrate newly developed DST methods using altered conditions. In vitro results of DST to second-line drugs were affected by criteria for measuring resistance such as the critical concentrations and critical proportions of drugs. For instance, DST with L-J solid media was established MICs that was defined as the drug concentration on which <20 colonies were found, while MIC in MGIT 960 was defined as the drug concentration at which the daily change in growth unit was less than that of the 1 : 100 control [17].

Worldwide public health programmes agree that tuberculosis (TB) remains a major challenge. Several national and international organizations have worked together for Tuberculosis control, and estimates of TB incidence, prevalence, and mortality are improving. Tuberculosis prevalence in 2010 was estimated at 178 cases per 100.000 people (95% CI, 156–201) worldwide [19-22]. Although substantial progress has been made, some conditions, especially related to noncommunicable diseases, still hinder the ultimate control of tuberculosis [2, 3]. Chronic kidney disease is one of these, and in kidney transplant subjects TB is an important opportunistic infection. Its frequency can be up 30 times greater among transplant recipients than in the general population [4, 23]. Kidney transplant subjects generally have reactivation of latent infections as the most common form of tuberculosis development and due to the clinical presentation of TB is not characteristic, with more extrapulmonary events and nonspecific symptoms, the diagnosis of active disease is usually delayed [5]. Mortality by Tuberculosis in kidney transplant population is the highest among subjects with post transplant TB, and kidney is the most frequently transplanted organ [6, 8, 21, 23]. The graft function can be compromised by both the direct effects of tuberculosis as a drug interactions, which complexes the management of those subjects [7, 9].

According to World Health Organization estimates, one-third of the world's population is latently infected with M. tuberculosis, and 10% of immunocompetent individuals will progress from latent to active tuberculosis infection within their lifetimes [1]. Detection and treatment of latent

tuberculosis infection (LTBI) remains a cornerstone of the strategy to reduce the incidence of active tuberculosis in the United States. Daily isoniazid therapy for six to 12 months has been shown to significantly reduce the risk of progression from latent to active tuberculosis infection [2, 16]. In the 1970's, several cases of fatal hepatotoxicity during isoniazid therapy for LTBI raised concerns regarding widespread isoniazid use and led to a reconsideration of its safety in older adults [3]. Subsequent studies of isoniazid toxicity have compared the risk of hepatotoxicity between adults less than and greater than 35 years of age [4–10], and a meta-analysis of these studies demonstrated a small but statistically significant increased risk of hepatotoxicity among adults greater than age 35 [11]. Because of these concerns, providers may be more reluctant to initiate isoniazid therapy in older patients with LTBI, particularly in the presence of comorbid illnesses [12, 17].

Less is known about the relationship of advancing age and isoniazid toxicity among adults in later decades of life, particularly when used in clinical practice outside of tuberculosis control programs or public health clinics. Furthermore, although isoniazid treatment is recommended for use in long-term care facilities as a component of infection control programs [13], prior epidemiologic studies of isoniazid toxicity have been limited to outpatient settings.

Tuberculosis causes enormous social and economic disruption and hampers nation's development [1, 2, 16]. India accounts for one-fifth of the global TB burden, with 1.8 million developing the disease each year and of them about 800,000 are infectious. Nearly 0.4 million are dying due to Tuberculosis annually which translates to two deaths every three minutes [3]. The disease is most prevalent in the age group of 15 to 54 years [4, 5], which is the highly economically productive period of an individual's life with important consequences for the household when the individual falls sick with Tuberculosis. Generally, burden of TB is measured by morbidity and mortality which are key considerations [6]. However, only focusing on morbidity and mortality effects provides an incomplete picture of the adverse impact of ill health on human welfare. In particular, the economic consequences of poor health can be substantial. Health "shocks," such as unexpected increases in health expenditure, reduced functional capacity, and lost income or productivity are often a primary risk factor for impoverishment [7, 8]. At a societal level, poor population health is associated with lower savings rates, lower rates of return on capital, and lower levels of domestic and foreign investment; all of these factors can and do contribute to reductions in economic growth [9]. Measurement of these various adverse impacts provides decision-makers to take appropriate policy decisions and also to provide another dimension of justification for worth of investment in TB control [10–12].

Therefore, this paper used the data as can be found in [14] for the empirical illustration.

However, the objectives of our study were to:
i. construction of a chronic tuberculosis hazard table ;

ii. Obtaining the expected period of acquired Tuberculosis to become chronic tuberculosis;

iii construction of confidence bound around the expected period.

Apart from demographic processes such as births, deaths, immigration, and emigration, that affects the size and composition of a population, but also the size of healthy population [14]. The timing of these processes also plays a critical role; a population with high juvenile mortality will have a very different structure from a population with high mortality in the post- reproductive years. Life tables are tables of data on survivorship and fecundity of individuals within a population. A standard method is to collect data on a cohort, or group of individuals all born in the same time period. Life tables constructed this way are called cohort life tables. They can then be used to determine age- or stage-specific fecundity and mortality rates, survivorship, and basic reproductive rates, which in turn can be compared from cohort to cohort enabling an analysis of their annual variation [4, 13].

Life tables are mainly used in describing age specific mortality and survival rate of population especially in actuarial science where it is called mortality or actuarial table, demography, epidemiology, biology and other fields.

2. Materials and Methods

2.1. The Data Used

The data for this paper is a secondary data obtained from the record and clinical department of University of Ilorin Teaching Hospital, Ilorin, Kwara State Nigeria. The information was on the patients who were diagnosed to be suffering from a lung disease called Tuberculosis. The disease is so dangerous that if there is no urgent and proper medical attention, the infected may die. The data available contain the information on the date of birth and the date of onset of the disease for twenty patients who were monitored over years as can be found in [15].Since this is a cohort life table that account for the actual mortality experience of tuberculosis patients right from the date of the onset of the disease to the death of the last member of the cohort. The available data were analyzed using SPSS version 15, Chicago Inc., IL, and USA. We obtained the length of time,x,Incidence rate, I_x, probability of developing the disease, probability of survivorship, number of years without the disease by the total cohort, L_x, total number of healthy years beyond age x, T_x and expectancy of an infected individual.

For length of time, we consider the period between the date of birth and the onset of the disease. To construct the life table, we assume the radix, l_o of 1000 persons (i. e l_x is inthousand).

2.2. Development of the Proposed Table (Tuberculosis Hazard Table)

In developing (chronic) tuberculosis hazards table, the main concern is the computation of the estimate of the probability of dying,Q_x, in the age interval, $x\ to\ x + 1$ from

the associated Age Specific Death Rate, M_x , probability of surviving P_x , in the interval $x\ to\ x + 1$ from the associated potential patients;

The procedures to follow in the construction are as follows;

Determine the time interval onset of the disease.

$$x\ to\ x + 1 \qquad (1)$$

Age Specific Death Rate (ASDR), also known as the mortality experience for each age group of the population or the incidence rate for period x, M_x;

$$I_x = M_x$$

$$I_x = \frac{ASDR}{Mortality\ Experience\ for\ Age\ x}$$

$$I_x = \frac{Number\ of\ death\ in\ the\ interval\ (x, x + 1)}{People\ aged\ between\ x\ to\ x + 1}$$

$$\frac{Number\ of\ people\ developing\ a\ disease}{Population\ at\ risk} = \frac{D_x}{P_x}\ or\ \frac{D_x}{L_x}$$

$$I_x = \frac{D_x}{P_x}\ or\ \frac{D_x}{L_x} \qquad (2)$$

$where \qquad P_x : is\ the\ people\ aged\ x\ at\ mid-$
$year\ calendar$

Calculate the probability of developing the disease.

$$Q_x = \frac{M_x}{1 + \frac{1}{2}M_x}$$

$$= \frac{2M_x}{2 + M_x}$$

$$= \frac{2I_x}{2 + I_x} \qquad (3)$$

Calculate the probability of surviving;

$$P_x = 1 - Q_x$$

$$= \frac{2 - I_x}{2 + I_x} \qquad (4)$$

Determine the number free at age x;

$$l_x \qquad (5)$$

Obtain number of years lived by the entire patients in the interval $(x, x + 1)$;

$$L_x = \frac{l_x + l_{x+1}}{2} \qquad (6)$$

Obtain total number of years lived beyond age x;

$$T_x = \sum_{j=x}^{\infty} L_x \qquad (7)$$

Compute the expectation of acquiring (developing) a disease, e_x;

$$where\ e_x = I \sum_{j=x}^{\infty} L_j / l_x$$

$$= \frac{T_x}{l_x} \qquad (8)$$

To derive the variance of expected period of acquiring occupational hazards,

If

$$e_x = \frac{T_x}{l_x} \qquad (9)$$

And

$$T_x = \sum_{j=x}^{\infty} L_x,$$

then;

$$e_x = I \sum_{j=x} \left(\frac{L_j}{l_x}\right) \qquad (10)$$

But

$$L_j = \frac{1}{2}(I_j + I_{j+1})$$

$$e_x = \frac{1}{2}\sum_{j=x}^{\infty} \frac{(I_j + I_{j+1})}{I_j}$$

$$= \frac{1}{2}\sum_{j=x}^{\infty} \frac{I_j}{I_j} + \frac{I_{j+1}}{I_j}$$

$$= \frac{1}{2}\sum_{j=x} 1 + P_j \qquad (11)$$

For $P_{j=}(I_{j+1})/I_j$

So, $V(e_x) = \frac{1}{4}(\sum_{j=x}^{\infty} V(1 + P_j)$

$$= Sec^2 x \qquad (12)$$

$$Sec^2 x = \frac{1}{4}\sum_{j=x}^{\infty} (P_j . Q_j)/I_j \qquad (13)$$

$$where\ Q_j = 1 - P_j$$

2.3. Derivation of Variance of Expected Period of Acquired Tuberculosis to Become Chronic Tuberculosis

If

$$e_x = \frac{T_x}{l_x} \qquad (14)$$

And

$$T_x = \sum_{j=x}^{\infty} L_j$$

$$e_x = \frac{\sum_{j=x}^{\infty} L_j}{l_x} \qquad (15)$$

But

$$L_j = \frac{1}{2}(l_j + l_{j+1})$$

$$e_x = \frac{\frac{1}{2}\sum_{j=1}^{\infty}(l_j+l_{j+1})}{l_j} = \frac{1}{2}\sum_{j=x}^{\infty}\left(\frac{l_j}{l_j} + \frac{l_{j+1}}{l_j}\right)$$

$$= \sum_{j=x}^{\infty} 1 + P_j \qquad (16)$$

For

$$P_j = \frac{l_{j+1}}{l_j}$$

So

$$V(e_x) = \frac{1}{4}\sum_{j=x}^{\infty} V(1 + P_j)$$

$$= Se^2_x \qquad (17)$$

$$= \frac{1}{4}\sum_{j=x}^{\infty} P_j(1 - P_j)$$

$$Se^2_x = \frac{\frac{1}{4}\sum_{j=x}^{\infty} p_j q_j}{l_j} \qquad (18)$$

Where

$$q_j = 1 - P_j$$

2.4. Construction of 100(1−∝)Confidence Interval for the Expected Length of Staying Before the onset Of Chronic Tuberculosis (e_0)

The $100(1 − X)\%$ confidence interval for e_0 is given by

$$e_0 \pm z_1 - \frac{\propto}{2} SE(e_0) \qquad (19)$$

3. Results

Table 1. Incidence rate of 20 patients.

X	D_x	l_x
0	-	0
1	-	0
2	-	0
3	1	0.05
4	4	0.2105
5	2	0.1333
6	5	0.3846
7	4	0.5
8	3	0.75
9	1	0.01

Table 2. The Life Table for the patients.

S/N	x	l_x	I_x	Q_x	P_x	L_x	T_x	e_x
1	3	1	.05	0.49	0.95	972	3796	3.796
2	4	.950	.21	0.20	0.80	858	2824	2.966
3	5	.760	.13	0.13	0.88	716	1966	2.577
4	6	.680	.38	0.32	0.68	561	1250	1.871
5	7	.450	0.5	0.40	0.60	363	689	1.521
6	8	.272	0.75	0.55	0.45	198	326	1.199
7	9	.124	1.0	0.6667	0.3333	83	128	1.032
8	10	.420	1.0	0.6667	0.3333	28	45	1.071
9	11	.140	1.0	0.6667	0.3333	10	17	1.214
10	12	.005	1.0	0.6667	0.3333	4	7	1.400
11	13	.002	1.0	0.6667	0.3333	2	3	1.500
12	14	.001	1.0	0.6667	0.3333	1	1	1.000

Table 3. Variance of Expected Period of Acquiring Chronic Tuberculosis.

x	e_x	P_xQ_x	$\frac{P_xQ_x}{l_x}$	S^2e_x	Se_x
3	3.796	0.046	4.6×10^{-5}	0.1006	0.3172
4	2.966	0.159	1.67×10^{-4}	0.1006	0.3172
5	2.577	0.109	1.43×10^{-4}	0.1006	0.3171
6	1.871	0.219	3.27×10^{-4}	0.1005	0'3170
7	1.521	0.240	5.31×10^{-4}	0.1004	0.3169
8	1.991	0.248	9.12×10^{-4}	0.1003	0.3167
9	1.032	0.220	1.77×10^{-4}	0.0996	0.3157
10	1.071	0.220	5.24×10^{-3}	0.1001	0.3164
11	1.214	0.220	1.59×10^{-2}	0.0983	0.3157
12	1.400	0.220	1.59×10^{-2}	0.0893	0.3136
13	1.500	0.220	0.111	0.0833	0.2885
14	1.000	0.220	0.222	0.0555	0.2356

Confidence Interval for e_x

$$e_3 = 3.796$$

$$e_0 = 3+3.796$$

$$= 6.796$$

Therefore, confidence interval for e_0 is given as

$$(6.7763, 6.8157) \qquad (20)$$

4. Discussion

We developed the table showing the incidence rate of tuberculosis patients in University of Ilorin Teaching Hospital using twenty (20) patients who had been monitored over years. The confidence interval for the expected period with the disease (Tuberculosis) but without developed to chronic tuberculosis was also given. This is desirable because there is the need for health education programs that will emphasize recognition, identification, and modification of risk factor for Tuberculosis.

The work demonstrates an algorithm to obtain the expected period before any chronic infectious hazard such as Tuberculosis sets in specifically, it was obtained that for the potential patient(s), the expected period of developing the Tuberculosis is 6.796 years before the infection become chronic infection (Tuberculosis).The 95% confidence interval for the estimated period was to be between 6.7763 and 6.8157.

5. Conclusion

The development of this estimation of the expected period of acquired chronic tuberculosis as health hazard has demonstrated an algorithm to obtain the expected period of

acquiring chronic tuberculosis and this would assist health policy maker to formulate policies that curb the pandemic of the disease.

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