



Evolutionary Trends for Pulmonary Tuberculosis Treatment Using DOTS in Sierra Leone: 1992-2010 Database Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author JBK protocol design, data analysis, writing and review of manuscript, first author. Author MK data analysis, literature reviews and questionnaire designing.

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ABSTRACT

Background: Sierra Leone started the Direct Observation Treatment Strategy (DOTS) for the treatment of pulmonary tuberculosis in 1992. The country's pulmonary tuberculosis (PTB) treatment program is now standardized according to international scale. Under the national standardized PTB treatment system, the regimen for new PTB patients consists of a 2-month intensive treatment phase with isoniazid, rifampicin, pyrazinamide and ethambutol, followed by a 4-month continuation phase with rifampicin and isoniazid.

Aims: To determine and analyse the annual PTB treatment success and incidence rates, treatment defaulters' rate, and pulmonary tuberculosis mortality from 1992 to 2002 under the DOTS program at the Germany Leprosy Relief Association's (GLRA) 13 regional diagnostic centers and chest clinics in Sierra Leone and to compare this data with the annual national tuberculosis data stored in WHO tuberculosis database covering the period 1992-2010.

Study Design: The study retrospectively analysed pulmonary tuberculosis annual incidence rates for study subjects who registered for diagnosis and later for treatment at the GLRA 13 regional diagnostic centers and chest clinics from 1992 to 2002. From

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these data we were able to determine the treatment success and defaulters' rates, and PTB mortality for these subjects. We also analysed data of the annual national tuberculosis incidence and success rates, and mortality rates retrieved from World Health Organisation (WHO) TB data for Sierra Leone for the period 1992-2010. Twenty six (26) healthcare service providers were also interviewed for additional information about the main cause of mortality and reasons for treatment defaults among pulmonary tuberculosis patients during the period under investigation.

Study Subjects: A total of 2,958 (1,881 men and 1,077 females) mostly adults of age range 15-65 years were diagnosed and later treated for pulmonary tuberculosis from 1992 to 2002 at the various GLRA diagnostic and treatment centers in the country.

Setting: The study was a multicenter study conducted at the Germany Leprosy Relief Association's (GLRA) main referral diagnostic center and chest clinic at Lakka in Freetown and the Department of Environmental Health Sciences, Njala University in Bo, Sierra Leone. Pulmonary tuberculosis treatment outcomes data used in this study were obtained from TB patients who were admitted at various GLRA chest clinics in Sierra Leone from 1991-2002. Data analysis and literature reviews were done at the Department of Environmental Health Sciences, Njala University in Bo, Sierra Leone from 2011 to 2012.

Results: The most important finding of this investigation was that the annual pulmonary tuberculosis incidence and treatment success rates (% cured rate and % completed treatment rate) rose significantly during the period under review for both the GLRA's study subjects and the cases stored in the WHO tuberculosis database.

Conclusion: The significantly high and growing number of annual PTB incidence rates during this HIV/AIDS epidemic reinforces the need for routine PTB treatment monitoring and supervision as well as compulsory HIV testing for tuberculosis patients seeking treatment.

Keywords: Prevalence; drug resistance; completed treatment; treatment defaulters.

1. INTRODUCTION

Pulmonary tuberculosis (PTB) is an infectious disease caused by *Mycobacterium tuberculosis*. The pathogen was first isolated in 1882 by Robert Koch and it commonly affects the lungs but can also involve almost any vital organ of the body [1]. Sierra Leone's PTB treatment is now standardized according to international scale. Under the national standardized PTB treatment program, the regimen for new patients consists of a 2-month intensive phase with isoniazid, rifampicin, pyrazinamide and ethambutol, followed by a 4-month continuation phase with rifampicin and isoniazid. However, the duration of treatment for active tuberculosis can be as long as 18 months and involves taking several different antibiotics. The most common medications used for active tuberculosis treatment previously in Sierra Leone were: isoniazid, rifampicin, streptomycin, and pyrazinamide. Ethambutol has now being added to the treatment regimen. In search of an affordable PTB treatment system that is also effective, Sierra Leone is now pursuing a phased implementation of the DOTS treatment strategy [2]. Under this new treatment system, PTB case finding is mostly passive with emphasis on intensive hospital-based treatment. The continuation phase of the treatment can also be provided on an out-patient basis, often at a general primary health care (PHC) facility. The duration of PTB treatment in Sierra Leone most times is extended at the discretion of the treating PTB specialists especially for those patients receiving hospital-based treatment following unsatisfactory physical and laboratory examinations results. Untreated person with active PTB will infect on the average between 10-15 people annually

[3]. A person with a compromised immune system like in the case of HIV infection is at high risk of becoming infected with TB [4]. The WHO estimated that one-third of the world's population is currently infected with the TB bacillus. Five to ten percent of people infected with TB but not infected with HIV become sick or infectious in their life time [5]. Southeast Asia has the highest number of estimated deaths from TB but Africa has the highest mortality per capita due to the increase in HIV [7]. The loss of life and human potential due to TB has surged in recent years as a result of coinfection with HIV.

2. METHODOLOGY

We reviewed and later analyzed the collated annual treatment outcomes records of 2,958 (1,881 men and 1,077 females) pulmonary tuberculosis patients of the age range 15-65 years who were diagnosed and later treated for the infection from 1992 to 2002 at the various GLRA chest clinics and treatment centers in the country (Table 1). Study subjects were all sputum smear positive PTB patients who were enrolled for pulmonary tuberculosis treatment in all 13 regional GLRA diagnostic centers and chest clinics in Sierra Leone from 1992 to 2002. From the records it was possible to determine the percentage of those PTB patients who completed treatment, defaulted treatment, totally cured, % PTB mortality, and treatment failures. Patient treatment records also noted the date of PTB diagnosis, initial sputum smear result, date of start of PTB treatment, and date of last drug intake. The ICD-10 (International classification of Disease) was used by GLRA for all PTB identification for this study. GLRA used culture diagnostic technique and sputum smear microscopy for tuberculosis diagnosis in all its regional chest clinics and diagnostics centers in Sierra Leone during the period under review. Most PTB chest clinics and diagnostic centers in resource-constraint countries rely on culture diagnostic technique for PTB diagnosis because it is sensitive and affordable. GLRA uses the culture PTB diagnostic technique also in order to differentiate between *Mycobacterium tuberculosis* from other non TB *Mycobacterium* pathogens such as *Mycobacterium leprae*. Sputum smear microscopy is also used in GLRA diagnostic centres nationwide because in spite of the fact that the technique is universal, it can effectively identify various *Mycobacterium* species. The technique is also significant because of the speed at which higher proportion of smear positive PTB cases are detected. Speed is significant during PTB diagnosis especially for the diagnosis of drug-resistance PTB cases-especially for TB drug resistance cases due to rifampicin which is now common in Sierra Leone. Imported PTB cases from outside Sierra Leone were excluded from this investigation since we cannot confirm whether such imported cases were reinfections or new PTB cases. This study also excluded imported PTB cases because PTB relapse cases are not included when determining the treatment success rate for tuberculosis. According to the WHO, tuberculosis treatment success rate is defined as the percentage of new registered smear positive cases that were cured or in which full course of tuberculosis treatment was completed. The WHO defined a new PTB patient as one who at the time of registration had never taken any treatment for tuberculosis, or had taken PTB treatment for less than one month [8]. We calculated the annual percentages of each component of the treatment outcome (treatment casualties, treatment defaulters, treatment failures, completed treatment, cured, and treatment failure).

The study also used secondary data of the annual national TB incidence and success rates, and tuberculosis mortality rate published by the World Health Organisation (WHO) for the period 1992-2010 to serve as national annual PTB update for comparative analysis purpose (Table 2).

We interviewed 26 healthcare service providers (two medical doctors, sixteen community health officers and eight laboratory technicians) to obtain additional information regarding the main cause of mortality and reasons for treatment defaults among pulmonary tuberculosis patients during the period under investigation. One advantage of this approach was that it provided useful information relating to PTB patients' treatment default thereby excluding a potential selection bias that is more prone to several earlier studies. Its thus enabled us to quickly obtain a general picture of the national tuberculosis situation in Sierra Leone with respect to the treatment outcomes of the infection; allowed us to identify the characteristics of the defaulters, as well as to fully identify the reasons for defaulting.

Table 1. Incidence, treatment defaulters, mortality and success rate for pulmonary tuberculosis in GLRA clinics between 1992-2002

Year	Incidence /1,000,000	Defaulters (%)	Mortality (%)	Success Rates (%)
1992	141	24.0	13.1	62.9
1993	203	30.3	12.6	57.1
1994	194	28.4	10.7	60.9
1995	202	23.3	11.8	64.9
1996	248	10.1	22.3	67.6
1997	271	12.1	19.2	68.7
1998	294	14.6	8.8	76.6
1999	314	8.1	15.4	76.5
2000	345	9.5	14.7	75.8
2001	362	18.1	6.9	75.0
2002	384	9.9	14.5	75.6
Total	2,958			

Table 2. Incidence, mortality and success rate for pulmonary tuberculosis, 1992-2010

Year	Incidence per 1,000,000	Success Rates (%)	Mortality TB (%)
1992	233	--	27.0
1993	248	--	26.0
1994	263	75	25.8
1995	279	69	25.4
1996	297	74	25.3
1997	315	79	25.0
1998	334	--	24.9
1999	355	75	24.5
2000	377	77	24.4
2001	400	80	24.3
2002	425	81	24.0
2003	451	83	23.7
2004	479	82	23.4
2005	509	86	22.9
2006	540	87	22.6
2007	574	89	22.3
2008	608	86	21.7
2009	644	79	21.9
2010	682	86	21.8

Source: WHO 2012⁶

3. RESULTS

A total of 2,958 (1,881 men and 1,077 females) of the age range 15-65 years were diagnosed and later treated for pulmonary tuberculosis from 1992 to 2002 at the various GLRA chest clinics and treatment centers in the country. The annual incidence rates for registered PTB patients who were diagnosed and later treated for the infection at the various GLRA regional diagnostic centers and clinics in Sierra Leone varies during the period 1992-2002. The median duration of treatment was 218 days for PTB patients who completed their treatment and got cured; and 76 days for defaulters. Majority (67%) of the treatment defaulters stopped taking their drugs during the intensive phase after a median treatment duration of 43 days; 13% defaulted during the continuation phase after a median treatment duration of 84 days. Twenty percent of study subjects completed the intensive phase but did not start the continuation phase; their median treatment duration was 64 days. The annual PTB incidences and treatment success rates among study subjects rose significantly from 1996 onwards.

According to the WHO annual national TB register for Sierra Leone (See Table 2) there was a progressive increase in the annual PTB incidence rates from 1992-2010. The highest (682) annual national PTB incidence occurred in 2010 while 1992 registered the lowest (233). Annual national pulmonary tuberculosis incidence rose significantly from 1996 upwards; annual national PTB incidence for 1996 was 297 but spiked to 334 in 1998– a 37% increase.

Pulmonary tuberculosis treatment success rate for the study subjects was highest (76.6%) in 1998 but lowest (57.1%) in 1993. There were no WHO registered annual national PTB treatment success rates for 1992, 1993 and 1998. 1997 recorded the highest (89%) annual national PTB treatment success rate while 1995 recorded the lowest (69%) for period 1992-2010.

1993 recorded the highest (30.3%) treatment default for tuberculosis treatment among study subjects while 1999 recorded the lowest (8.2%). The highest (22.3%) mortality rate among study subjects for the period under review was registered in 1996. The lowest (6.9%) mortality rate for study subjects was registered in 2001. 2010 recorded the lowest (21.7%) PTB mortality according to the WHO annual PTB statistics for the period under review while 1992 registered the highest (27%). PTB mortality among study subjects was highest (22.3%) in 1996 but lowest (6.9%) in 2001 for the period 1992-2010,

Majority (98%) of the healthcare service providers blamed PTB treatment default on high pill burden during the intensive hospital-based phase of treatment. Ninety-seven percent of healthcare service providers say few (2%) PTB patients blamed lack of regular family and friends' visits in addition to high pill burden for hospital-based PTB treatment prone to high treatment default. All (100%) healthcare service providers say majority (98%) of PTB patients treatment defaulters did not really default but continued PTB treatment under 'non-DOTS' conditions were they are not further evaluated neither directly observed like those under the strict DOTS treatment strategy.

4. DISCUSSION

The main strengths of this study are that it is a large population based study; it encompassed a long period (18 years) which offered the opportunity for investigators to be able to assess long term incidence, treatment success and mortality trends; and it made use

of medical linked records that incorporated systematic follow up of the patients. The most noteworthy findings of this investigation are the annual increase in the PTB treatment success rates (% of completed treatment and % cured) and the annual progressive increase in the incidence rate of the infection during the period under review. The increase in annual treatment success rate for PTB during the period under review could be associated with the introduction of the bacteriostatic drug ethambutol as one of the components of the treatment regimen alongside bactericidal drugs such as isoniazid, streptomycin, pyrazinamide and rifampicin. Sierra Leone started using ethambutol as part of the PTB treatment regimen in 1998 [9].

The treatment success rates for PTB prior to the introduction of ethambutol in 1998 were 62.9 %, 57.1%, 60.9%, 64.9%, 67.6% and 68.7% for 1992, 1993, 1994, 1995 1996, and 1997 respectively. Pulmonary tuberculosis treatment success rates shots above 70% from 1998 and beyond. An increase in the PTB treatment success rate implies a concomitant drop in the treatment failure rate.

Pulmonary tuberculosis treatment failure is mostly associated with treatment default, unavailability of drug and drug resistance which in turn can be associated with poor drug quality, improper or incorrect drug dosage and the over dependence on a particular set of PTB drugs. Most PTB patients who failed chemotherapy in Sierra Leone during the period under review initially depended on isoniazid, streptomycin, pyrazinamide and rifampicin which were the affordable drugs at the time. Most emerging drug-resistance *Mycobacterium* spp are associated with the over dependence on isoniazid, streptomycin, pyrazinamide and rifampicin. Between 1992 to 1998 bactericidal drugs like isoniazid, streptomycin, pyrazinamide and rifampicin were the drugs of choice in Sierra Leone for PTB treatment mostly because of their cost and partly because of the lack of access to other highly effective PTB drugs. The over dependence on these bactericidal drugs may have thus resulted into unusually high annual PTB incidences (new cases) and hence prevalence (total cases) in a given locale since there is the likelihood of the building up of drug resistance *Mycobacterium tuberculosis* pathogens population that are able to withstand such drugs and which were later transmitted to non infectious human. Most pulmonary tuberculosis treatment default is related to high pill burden and types of PTB healthcare service. Tuberculosis treatment strategies that require the taking of large cocktail of drugs at specific intervals are most likely not to be completed than treatment regimens that require few drugs only. This is supported by the fact that 67% of the PTB treatment defaulters stopped taking their drugs during the intensive phase of their treatment and after a median treatment duration of 43 days. The national standardized DOTS pulmonary tuberculosis treatment program consists of a 2-month intensive treatment phase with isoniazid, rifampicin, pyrazinamide and ethambutol under strict hospital monitoring and supervision. Also, the low treatment rates for pulmonary tuberculosis from 1991 to 1997 can be explainable to the fact that, PTB treatment in Sierra Leone prior to 1998 requires a cocktail of drugs like isoniazid, streptomycin, pyrazinamide and rifampicin which has to be taken for more than 12 months to ensure complete treatment and cure. This drug regimen proved cumbersome and time consuming for most tuberculosis patients at the time and most often resulted into PTB treatment default and hence treatment failure when they were not monitored properly. A high treatment default can also be the result of the socioeconomic and political climate in the country at the time. During the period 1992 to 1998, Sierra Leone's political and security climate were very unstable and unreliable. A rebel war that broke out in the country in 1991 had spread throughout the entire 13 regions of the country creating a massive movement of internally displaced persons across the country. War creates a climate of instability and constant human movement which makes it difficult for people to complete their pulmonary tuberculosis treatment. Pulmonary

tuberculosis treatment default and hence its subsequent treatment failure increases as a result of high human movement. Sierra Leone's healthcare system as well as factors relating to hospitalized PTB patients also tends to support high PTB treatment default. This is justified considering the responses obtained from the various PTB healthcare service providers interviewed during this investigation. This study interviewed 26 healthcare service providers to obtain plausible reasons and suggestions that will help to explain the main causes that are responsible for mortality and tuberculosis treatment default among the study subjects. Majority (98%) of the healthcare service providers interviewed gave as reason for treatment default, high pill burden as one of the major reasons PTB patients refused their treatment continuation. Ninety percent of healthcare service providers interviewed say most (83%) PTB patients enrolled in this study complained of lack of regular family and friends' visits as primary reason that makes hospital-based PTB treatment in Sierra Leone prone to high treatment default. All (100%) healthcare service providers interviewed say majority (65%) of PTB patients treatment defaulters did not really default but continued TB treatment under 'non-DOTS' conditions were they are not further evaluated neither directly observed like those under the strict DOTS treatment strategy making such TB treatment defaulters a high risk group.

These reasons proffered by these healthcare service respondents are justified considering the fact that hospital-based PTB intensive phase treatment is highly monitored for treatment compliance. The problem of the lack of strict pulmonary tuberculosis treatment monitoring and compliance is further compounded considering the fact that hospital-based PTB treatment duration is also usually longer than the intensive phase of the ambulatory-based treatment that is not monitored. These non-DOTS' group; mostly unemployed youths of the age 18-35 years; and mostly men are a high risked group primarily because of their irregular and disruptive treatment pattern due to their urge to search for food, income and sometimes to satisfy their life styles. Irregular and inappropriate drug regimen coupled with disruptive tuberculosis treatment process increases the possibility of the emergence of tuberculosis drug-resistance strains during TB treatment which also invariably affect the treatment success rate. This study tends to support previous investigation about the contribution and importance of ambulatory-tuberculosis treatment program on the impact of the treatment outcomes [10] compared to the intensive-hospitalized (sanatorium style) PTB treatment option.

5. CONCLUSION

Pulmonary tuberculosis in Sierra Leone is a national public health crisis in the wake of the HIV/AIDS pandemic. Pulmonary tuberculosis treatment default during the study period occurs mostly during the intensive phase when patients are hospitalized. A number of risk groups (unemployed male youths, pensioners, homeless and alcoholics mostly of the age range 18-35 years) have been identified that require special attention. An obligatory intensive phase PTB treatment coupled with a weak system of patient transfer to the general primary health care (PHC) facilities upon completion of the intensive-hospitalized treatment phase are important system factors that leads to PTB treatment default in Sierra Leone. Pulmonary tuberculosis treatment default can be substantially reduced by shortening the duration of the intensive phase of patient treatment, increase monitoring and supervision at the ambulatory continuation treatment phase at various PHC facilities in the Sierra Leone, and the improvement of the referral system between in-patient facilities and PHC services. The DOTS treatment program in Sierra Leone can be made to be more successful if the number of drugs taken during the intensive phase is reduced but the period for the intensive phase of treatment extended. The National Tuberculosis and Leprosy Control Program

(NTLCP) should also provide enough support to ambulatory tuberculosis treatment program since the treatment outcomes for outpatient tuberculosis patients is more favorable than that of the intensive hospitalization treatment program for tuberculosis patients.

CONSENT

All authors declared that a written informed consent letter was obtained from authorities of the Sierra Leone National Tuberculosis and Leprosy Control Program (NTLCP) prior to the commencement of data collection for this study.

ETHICAL APPROVAL

All authors hereby declared that all procedures relating to this study was approved by the appropriate ethics committee of the Department of Environmental Health Sciences, Njala University, Sierra Leone and GLRA.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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