Impact of the Ebola virus disease outbreak (2014-2016) on Tuberculosis Surveillance Activities in Guinea's National Tuberculosis Program: A Time Series Analysis

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Abstract

Background

Tuberculosis (TB) is a major cause of disease and death worldwide. According to estimates published by WHO, Guinea is one of the countries with a high incidence of tuberculosis and tuberculosis / HIV co-infection. In March 2014, the World Health Organization (WHO) announced the Ebola virus disease outbreak in Guinea that caused a health system disruption. Our study aimed to assess the impact of the Ebola virus disease outbreak on the TB surveillance system through the main indicators of TB-related morbidity and mortality.

Methods

This is a retrospective cohort study by comparing TB trends through TB surveillance data from periods before (2011-2013), during (2014-2015) and after (2016-2018) the Ebola virus disease outbreak. A time-series analysis was conducted to investigate the link between the decrease in TB incidence and the Ebola virus disease through cross-correlation. We evaluated the surveillance system to compare its current status with that of the Ebola virus disease outbreak period.

Results

The reporting rate for TB cases has decreased from 120 cases per 100,000 people reported in 2011 to 100 cases in 2014. The cross-correlation test between TB and the Ebola virus disease incidents shows a significant lag of -0.6 (60%) this corresponds to the drop in TB incidence observed when Ebola virus disease was at its peak in 2014.

Concerning the surveillance system, of the 13 standards, only five are reached in 2019 compared to 3 in 2015.

Conclusion

The Ebola virus disease outbreak has had a severe impact on TB surveillance in Guinea.
The introduction of an early warning system would preserve the TB surveillance system; which could encourage the implementation of set stakes to ensure access to diagnosis, treatment for enhanced surveillance of tuberculosis.

Introduction

Although it can be 100% cured, tuberculosis remains the second leading cause of death from infectious diseases worldwide, with multi-drug resistant TB becoming more common(1). This disease is a priority of the Ministry of Health of the Republic of Guinea, which listed it as a disease under surveillance by creating the National Tuberculosis Control Program in 1990(2). In 2014, the Guinean government aligned its tuberculosis control policy with WHO’s proposed TB strategy, developed in conjunction with the Sustainable Development Goals. Efforts have been made to align indicators and targets in the context of underdevelopment (3).

The Ebola virus disease outbreak between 2014 and 2015 had an impact on all health activities. It has been the most severe and durable in history, mainly affecting West African countries (Guinea, Sierra Leone, and Liberia). The Ebola outbreak in West Africa in 2013-16 was unprecedented in the number of cases, deaths, and survivors (5). Guinea reported a total of 3,811 cases of Ebola and 2,543 deaths nationwide during the outbreak. In addition to the devastating health effects, the Ebola virus disease outbreak has also had a significant socio-economic impact in Guinea, Liberia, and Sierra Leone(6). According to World Bank forecasts for 2014(7), it is estimated that $2.2 billion was lost in 2015 in the gross domestic product (GDP) of the three countries.

Before the Ebola virus disease outbreak, the Guinean health system was in difficulty and was severely shaken during the Ebola virus disease outbreak, the main problem being the lack of infrastructure and skilled workers. With a population of more than 11 million, the country had only one doctor and one nurse per 10,000, 25 times less than in the United
States. This low ratio of health care providers to the population deteriorated further due to the high rate of Ebola infections and deaths among health care workers (192 Ebola infections, including 86 deaths).

Based on these findings, we hypothesized that the Ebola virus disease outbreak has led to an increase in TB-related morbidity and mortality as a result of the blow to the TB surveillance system. Which leads us to ask the following question: what are the main effects of the Ebola virus disease outbreak on TB indicators? Our study aimed to assess the impact of the Ebola virus disease outbreak on TB surveillance activities.

Materials And Methods

Location and period of study

The study was carried out at the NTP of the Republic of Guinea from February 2019 to June 2019. This program is the responsibility of the National Directorate of Great Endemics, which is attached to the Ministry of Health. This direction is the main body responsible for epidemiological surveillance of tuberculosis, notification, and treatment of TB cases.

Study design and population

We conducted a retrospective cohort study by comparing TB trends through routine TB control data from periods before (2011-2013), during (2014-2015) and after (2016-2018) of Ebola virus disease. The data for these periods were extracted from the national health information management system based on the DHIS2. The NTP provides this database for TB surveillance data. We also assessed the current state of the surveillance system compared to the 2015 assessment during the Ebola virus disease outbreak.

Data used

The overall TB surveillance data used in this study were extracted from the National Health Information System (DHIS2), which contains a module for the collection and analysis of TB data. Tuberculosis cases are collected and reported from the diagnostic and
treatment centers available in all health districts. TB surveillance reports were collected and quarterly captured in the DHIS2 set up in 2016. Historical aggregate surveillance data (2009–2015) of the NTP have been imported into this system, and data entry continues at the national level.

We have included all comprehensive epidemiological surveillance data recorded in the National Surveillance System (DHIS2) from 2011 to 2018. However, unregistered paper statements and data from some diagnostic and treatment centers that were not communicated to the NTP were excluded.

Population estimates were obtained from the National Statistics Institute (NSI), which conducted a general population census in 2014 and projected the population for subsequent years to 2020. The Ebola virus disease outbreak surveillance data were obtained from the National Health Security Agency (NHSA), which monitors epidemics in the country.

**Operational definition of variables**

The variables in our study are collected at the base by quarterly report forms completed by practitioners. The calculated indicators from these variables are based on the NTP contractual programmatic indicators and are in line with the new WHO revised definitions for 2013. We have targeted two sets of indicators: indicators for reporting TB cases and those for treatment outcome.

**Indicators for case notification**

Tuberculosis case notification rate: is the number of reported TB cases per 100,000 population. This rate is also calculated according to the clinical forms (bacteriologically confirmed and diagnosed clinically)

**Indicators for therapeutic outcomes**

Therapeutic success rate: is the ratio of the number of patients who have completed treatment to the total number of reported patients.
Relapse rate: is the ratio of the number of relapses detected on the number of TB cases confirmed bacteriologically.
Rate of loss of sight: this is the ratio of the number of confirmed TB cases bacteriologically and clinically
who have not started treatment, or it has been discontinued for at least two consecutive months out of the total number of TB cases Registered. The accepted standard of this rate is less than 5%. Death rate: this is the ratio of the number of TB deaths confirmed bacteriologically during treatment, and regardless of the cause of the total number of TB cases confirmed bacteriologically. Rate of non-assessed: this is the ratio of the number of unassessed cases to the total number of TB cases.

Statistical analysis plan

A description of the overall epidemiological situation of tuberculosis was carried out over all three periods using the notification rates per 100,000 inhabitants, frequencies related to the population. We used the WHO standards and criteria for the evaluation of TB surveillance systems to assess the status of the current surveillance system compared to the 2015 assessment during the Ebola virus disease outbreak.

A time-series analysis was conducted to assess the effect of Ebola virus disease on the notification and treatment of TB cases. To do this, we used the autocorrelation coefficient to examine the significance of the shifts observed in each time series separately and the cross-correlation coefficient explore the relationship between the time series of Ebola and those of tuberculosis. Although there are currently meaningless correlations between independent time-series pairs that are themselves auto-correlated, the link between these two time-series can be explained by the correlation coefficient provided that the two stationary series, \{xt\} and \{yt\}, are independent of each other (that is, if the values of a time-series at a given moment do not provide any information about the values of the other time-series at a given moment) (8).

The stationarity tests can check whether a series is stationary or not, we used the Dickey-Fuller test which is a unit root test for which the Ho hypothesis is that the series is stationary and then we transformed seasonal series in stationary series (9).

Stationarity is defined by a constant average and equal variance at any time and can be obtained by diversion or differentiation. Differentiation is the sequential subtraction of the xt value of xt +1 from a time series to get subsequent changes over time (8). Stationarity
is a prerequisite for modeling and removes spurious correlations based on time
dependencies between adjacent values in the input time series and removes these
influences from the output time series(10). The DHIS2, Excel, and R 3.5.1 software was
used for data analysis.

Results
In Guinea, the NTP tuberculosis case notification rate decreased from 120 cases per
100,000 population in 2011 to 100 cases per 100,000 of the population in 2014, resuming
an upward trend after 2015 (Figure 1). From 2012 to 2013, the trends were down slightly,
but higher than in 2014. After this year, notifications of new cases and relapses for all
forms of TB started to increase. The same is true for new clinically diagnosed cases,
pulmonary relapses, and clinically confirmed cases and pulmonary relapses. The recovery
of the upward trend just after the historic decline recorded in 2014 is very evident and
continues to increase each year (Figure 1).

From 2011 to 2014, notification rates for both all forms of TB cases, bacteriologically
confirmed and clinically diagnosed pulmonary cases showed negative variations, i.e., a
decrease in the number of cases detected each year with a peak of –26 for
bacteriologically confirmed TB cases in 2014. As of 2015, annual changes ranging from 7%
for new TB cases clinically diagnosed to 17% for TB cases bacteriologically confirmed
(Figure 4).

About the tuberculosis surveillance system, out of 13 standards and criteria developed by
WHO, five were reached by the NTP in 2019 compared to only 3 in 2015 (Table 3). This
means that the surveillance system deserves targeted, long-term action to meet the
challenge of screening and monitoring patients on treatment.

The analysis of the time series of NTP notifications shows essentially a gap with a much
larger trough between 2014 and 2015. From 2011 to 2018, cascades are observed over
the years concerning the reported cases of tuberculosis in all forms in the range of 2000 to 4000 cases per quarter and vary from year to year. The periods between 2014 and 2015 are those for which, it is notified the lowest rates (2000 cases) compared to other years that recorded at least 2500 cases (Figure 2).

For Ebola cases, if the number of cases is less than 2200, except for the period of July 2014 which records up to 4000 cases, the data for TB cases of any reported form vary from year to year. These variations, much more marked by a decrease in 2014, would be based on the availability of providers, access to the service, and the choice of patients because of the epidemic context. Thus, between July 2014 and January 2015, fewer cases (2,200) were reported than in January and July 2014 (more than 3,000), this highlights a decline in the Ebola rate.

By examining reported cases of tuberculosis in all forms, data are available for almost all years and above 2,500 cases per quarter, but these trends were down in 2014. After an increase of more than 3000 this year, a drop-off point is again observed shortly before 2015, when Ebola cases will see a sharp increase.

The success rate has gradually increased over the years, despite the severity of the Ebola outbreak. The diagnosed patients were followed and put on TB treatment. Outcome indicators did not vary sufficiently during the epidemic period; the success rates range from 76% to 94% for all years (table1).

The Ebola incidence evolved rapidly to acme and then declined, with the most significant proportion recorded before 2014 (more than 500 cases). The incidence of tuberculosis, meanwhile, decreased by –1500 cases between 2014 and 2015 before fluctuating the following year positively and then remaining until 2016.

The analysis of auto-correlation curves for the incidence of tuberculosis and Ebola does not show any significant lag for bacteriologically confirmed TB cases, the therapeutic
success rate, and the Ebola success rate, although all are independent but not seasonally adjusted (Figure 3). After converting these series to stationary time series, the cross-correlation test between the time series of tuberculosis and Ebola shows a significant lag of -0.6 (60%) for all forms of TB, which corresponds to the sharp decline in the incidence of TB seen at the height of the Ebola outbreak in 2014 (Figure 4). However, no significant lag is observed in the cross-correlation test for the therapeutic success rate an Ebola times series despite seasonal adjustment of the time series (Figure 4).

Discussion

Although WHO estimates the increase in the number of cases each year, however, the number of TB cases reported by the NTP remain low compared to these estimates. NTP notifications have declined considerably during the Ebola epidemic experienced by the country. Some tuberculosis treatment centers have been transformed into a health center for Ebola patients, which has resulted in a weakening of TB service provision in some places. A recent systematic review of the link between the Ebola epidemic in West Africa and the health systems in Guinea, Liberia, and Sierra Leone (11) revealed the poor performance of health facilities, in part because of the lack of staff in these health facilities during the epidemic, inadequate funding for health, lack of monitoring and communication. A study in Sierra Leone (12) also reported a break in the relationship between the health system and communities during the Ebola outbreak, resulting in a significant and significant reduction in the use of health facilities.

According to our study, the reporting rate of tuberculosis cases in the NTP increased from 120 cases per 100,000 population in 2011 to 100 per 100,000 in 2014, while the case of Ebola is the highest. Similar results were revealed by the study on the impact of Ebola on the results of tuberculosis screening and treatment in Liberia. This study showed that for all forms of tuberculosis stratified by category and by age group, significantly more
substantial decreases were observed in the last two quarters of 2014 (13).

Rashid et al. also indicated that the Ebola virus disease outbreak in West Africa had a significant impact on all sectors of the health system, mainly TB control services, which have increased the transmission of TB, morbidity and decreased adherence to antituberculous treatment (14).

The decrease in the number of TB cases reported during the Ebola virus disease outbreak may also have links to sociodemographic and behavioral factors resulting from the epidemic. Zachariah et al. cited the death of health workers, the temporary or permanent closure of health facilities and the inherent fear of contracting the Ebola virus or being stigmatized as a demographic factor influencing TB control (15).

Despite the blow to tuberculosis reporting by the Ebola virus disease outbreak, the therapeutic success rate has remained stable with little upward variation over 80%. This fact confirms the fact that TB cases that had been diagnosed had been followed closely during the Ebola virus disease outbreak in Guinea although these results are similar to those of several other studies (11,14,16), including one in Guinea (13), which had a higher success rate during the Ebola virus disease outbreak (80–87% for new cases of tuberculosis and a success rate varying between 72% and 80% for co-infected patients.

Besides, our data show that reporting rates for new cases and relapses for all forms of TB began to rise immediately after the 2014 decline. This post-Ebola performance is due to the positive effects of post epidemic, with improved diagnostic capacity by the new GeneXpert devices converted for TB screening. The same return of services after the outbreak was also noted by a study on the public health impact of the 2014–2015 Ebola virus disease outbreak (17). It reports that despite its adverse effects on public health and beyond, the Ebola outbreak has provided West African countries with many opportunities that have enabled Guinea to increase health expenditure, recruit an additional 2,950
health workers and begin to prioritize community participation in addressing public health threats(18).

Decreases in reported tuberculosis cases may be due to randomness or misinterpretation if statistical tests are not available. Cross-correlation tests between the Ebola virus disease outbreak and tuberculosis time series confirmed that the contagious decline was statistically significant with offsets beyond the confidence intervals of the cross-correlation curve. The incidence of tuberculosis dropped from ~1500 cases in 2015 before fluctuating the following year, and continued until the end of the Ebola virus disease outbreak in 2016.

Conclusion

Our study shows a near-general decline in TB notification rates for all forms between 2014 and 2016 during the outbreak of the Ebola virus outbreak and significantly. This trend is similar for new cases and clinically confirmed pulmonary and bacteriological relapses, as well as those that are pulmonary and clinically diagnosed. This, as evidenced by the results of the cross-correlation analysis, can be attributed to the MVE epidemic that has shaken the entire health system. Ebola virus disease outbreak, however, had no impact on the outcome of treatment of patients followed during the same period.

Declarations

Ethics approval and consent to participate

This study used aggregated surveillance data for tuberculosis and Ebola. The authorization of the Tuberculosis Control Program in Guinea was obtained for the analysis of the data.

Consent for publication

Not applicable

Availability of data and materials

The data is available upon authors request.
Competing interests
The authors declare that they have no competing interest in relation to this work.

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Author’s contributions
MAS conceived the study design, analyzed the data, and drafted the manuscript, BDD contributed to the conception, organization the research project, supervision data collection, drafting and critical revision to manuscript, SC, LMC, OYS, AMB, contributed to the conception, organization the research project, and critical revision to manuscript, BB, AOB, THD, LM, and AC commented the manuscript. All authors approved the final version of the manuscript.

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References
1. Frieden TR, Brudney KF, Harries AD. Global Tuberculosis: Perspectives, Prospects, and Priorities. JAMA [Internet]. 2014 Oct 8 [cited 2019 Mar 14];312(14):1393–4. Available from: https://jamanetwork.com/journals/jama/fullarticle/1901679

2. Programme National de Lutte anti-tuberculeuse. Plan strategique de lutte antituberculeuse en Guinee 2015–2019. 2016.

3. Lönnroth K, Raviglione M. The WHO’s new End TB Strategy in the post-2015 era of the Sustainable Development Goals. Trans R Soc Trop Med Hyg [Internet]. 2016 Mar 1 [cited 2019 Mar 14];110(3):148–50. Available from: https://academic.oup.com/trstmh/article/110/3/148/2578692

4. WHO. Maladie à virus Ebola [Internet]. 2018 [cited 2019 Mar 14]. Available from:
5. Deen GF, McDonald SLR, Marrinan JE, Sesay FR, Ervin E, Thorson AE, et al. Implementation of a study to examine the persistence of Ebola virus in the body fluids of Ebola virus disease survivors in Sierra Leone: Methodology and lessons learned. PLoS Negl Trop Dis [Internet]. 2017 Sep 11 [cited 2019 Mar 14];11(9). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5593174/

6. CDC. Cost of the Ebola Epidemic | 2014–2016 Outbreak West Africa | History | Ebola (Ebola Virus Disease) | CDC [Internet]. 2019 [cited 2019 Mar 14]. Available from: https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/cost-of-ebola.html

7. The World Bank. GDP growth (annual %) | Data [Internet]. 2017 [cited 2019 Mar 14]. Available from: https://data.worldbank.org/indicator/NY.GDP.MKTP.KD.ZG

8. Probst WN, Stelzenmüller V, Fock HO. Using cross-correlations to assess the relationship between time-lagged pressure and state indicators: an exemplary analysis of North Sea fish population indicators. ICES J Mar Sci [Internet]. 2012 May 1 [cited 2019 May 10];69(4):670–81. Available from: https://academic.oup.com/icesjms/article/69/4/670/632477

9. Patel AX, Kundu P, Rubinov M, Jones PS, Vértes PE, Ersche KD, et al. A wavelet method for modeling and despiking motion artifacts from resting-state fMRI time series. NeuroImage. 2014 Jul 15;95:287–304.

10. Dean RT, Dunsmuir WTM. Dangers and uses of cross-correlation in analyzing time series in perception, performance, movement, and neuroscience: The importance of constructing transfer function autoregressive models. Behav Res Methods [Internet]. 2016 Jun 1 [cited 2019 May 9];48(2):783–802. Available from: https://doi.org/10.3758/s13428-015-0611-2

11. Shoman H, Karafillakis E, Rawaf S. The link between the West African Ebola outbreak
and health systems in Guinea, Liberia and Sierra Leone: a systematic review. Glob Health [Internet]. 2017 Jan 4 [cited 2019 Sep 6];13. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5210305/

12. Elston JWT, Moosa AJ, Moses F, Walker G, Dotta N, Waldman RJ, et al. Impact of the Ebola outbreak on health systems and population health in Sierra Leone. J Public Health [Internet]. 2016 Dec 2 [cited 2019 Sep 6];38(4):673-8. Available from: https://academic.oup.com/jpubhealth/article/38/4/673/2966926

13. Ortuno-Gutierrez N, Zachariah R, Woldeyohannes D, Bangoura A, Chérif G-F, Loua F, et al. Upholding Tuberculosis Services during the 2014 Ebola Storm: An Encouraging Experience from Conakry, Guinea. PLoS ONE [Internet]. 2016 Aug 17 [cited 2019 Sep 6];11(8). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4988783/

14. Ansumana R, Bonwitt J, Stenger DA, Jacobsen KH. Ebola in Sierra Leone: a call for action. The Lancet [Internet]. 2014 Jul 26 [cited 2019 Sep 6];384(9940):303. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140–6736(14)61119–3/abstract

15. Sylvester Squire J, Hann K, Denisiuk O, Kamara M, Tamang D, Zachariah R. The Ebola outbreak and staffing in public health facilities in rural Sierra Leone: who is left to do the job? Public Health Action [Internet]. 2017 Jun 21 [cited 2019 Sep 6];7(Suppl 1):S47-54. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5515564/

16. Konwloh PK, Cambell CL, Ade S, Bhat P, Harries AD, Wilkinson E, et al. Influence of Ebola on tuberculosis case finding and treatment outcomes in Liberia. Public Health Action. 2017 Jun 21;7(Suppl 1): S62-9.

17. Elston JWT, Cartwright C, Ndumbi P, Wright J. The health impact of the 2014–15 Ebola outbreak. Public Health [Internet]. 2017 Feb 1 [cited 2019 Sep 6];143:60–70. Available from: http://www.sciencedirect.com/science/article/pii/S0033350616303225
18. Delamou A, Delvaux T, El Ayadi AM, Beavogui AH, Okumura J, Van Damme W, et al. Public health impact of the 2014–2015 Ebola outbreak in West Africa: seizing opportunities for the future. BMJ Glob Health [Internet]. 2017 Mar 16 [cited 2019 Sep 6];2(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5435258/

Tables

Due to technical limitations, Tables 1 - 3 are only available for download from the Supplementary Files section.

Figures

*Figure 1. TB and Ebola incident cases*
Figure 1

TB and Ebola incident cases

Figure 2. Tuberculosis all forms incident cases (2011-2018) VS Ebola cases, 2014-20162
Figure 2

Tuberculosis all forms incident cases (2011-2018) VS Ebola cases, 2014-2016
Figure 3

Auto-correlation of the seasonally adjusted series of TB incidence and Ebola virus disease
Figure 4. Cross-correlation test of tuberculosis and Ebola time series

Supplementary Files

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Table 2.pdf
Table 3.pdf
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