

One-year study on molecular diagnosis of drug-resistant tuberculosis among presumptive tuberculosis patients attending Direct Observed Treatment Shortcourse Clinics in Katsina State, North West, Nigeria

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ABSTRACT: Nigeria is one of the 24th high burden countries with drug resistant tuberculosis (DR-TB). This study aimed at determining the prevalence and factors associated with drug-resistant tuberculosis among presumptive tuberculosis patients attending Direct Observed Treatment Shortcourse centres in Katsina State, Nigeria. A one-year retrospective study of presumptive patients screened for *Mycobacterium tuberculosis* (MTB) and Rifampicin resistant (RR-TB) tuberculosis using Xpert MTB/RIF assay at 14 Genexpert sites in the State between January 1st, 2018 and December 31st, 2018 was conducted. A total of 14,501 presumptive patients were screened for MTB and Rifampicin resistant tuberculosis. The majority (51.4%) were between 25-44 years. Male: Female ratio was 1:0.8. Of the 14,501 clients screened, MTB was detected in 1,750 (12.1%) out of which 35 (0.2%) had DR-TB; Males 30 (0.2%), females 5 (0.03%) respectively. Age (AOR 1.8, 95%CI 1.3-2.6, p = 0.001), symptomatic contact with DR-TB patients (AOR 3.3, 95%CI 2.1-5.1, p. Drug-resistant tuberculosis is in existence in the study area with the prevalence of 0.2%. Drug resistant tuberculosis among presumptive TB patients was high in this study; therefore, urgent steps are needed to avert an impending DR-TB epidemic in the studied area.

Keywords: Tuberculosis, Drug-Resistant tuberculosis, Xpert MTB/RIF, Katsina State, Nigeria.

INTRODUCTION

Tuberculosis is an ancient disease, which has co-existed with humans throughout the evolutionary history. Evidence for tuberculosis disease is confirmed by phenotypic and molecular methods, which was found in skeletons dating to the Neolithic era (IUATLD, 2018). Approximately 9,000 years ago in eastern Mediterranean; however, some places estimated the origin of the disease (Comas *et al.*, 2013). This disease killed more people than any other disease throughout the world history (WHO, 2014). The

incidence reached its peak in the 19th century when a quarter of Europeans were thought to have died as a result of tuberculosis (WHO, 2014). Robert Koch made his famous presentation in 1882 in Berlin, where he demonstrated that the tubercle bacillus was the causative agent of tuberculosis. Koch's postulates which set the standards of infectious disease etiology, is still relevant today (IUATLD, 2018). One third of the world population is thought to be infected with tuberculosis, with an estimated

1.3 million death in 2012 (WHO, 2013), in addition to that TB/HIV co-infection and antibiotic resistance has raised this threat to both the developed and developing countries (WHO, 2012). The emergence of drug-resistant tuberculosis (DR-TB) is defined as resistance to at least one first line anti-TB drugs; this caused a major obstacle to TB control programme in Nigeria (Mohammad *et al.*, 2017). World Health Organization (WHO) reported that, 580,000 new cases of drug-resistant tuberculosis (DR-TB) were identified in 2015 and an estimated 250,000 DR-TB patients died (Adejumo *et al.*, 2018). Surveillance data shows that, about 4% of new and 21% of previously treated TB cases had DR-TB in 2015 (Cresswell *et al.*, 2018). There has been an increase in TB and DR-TB case notifications, the gaps in case detection and treatment remain due to under reporting and under diagnosis in developing countries (Mohammad *et al.*, 2021a). Nigeria ranked sixth position among the highest TB countries in the world and it is one of the 14 countries with the high burden of MDR-TB and TB/HIV co-infection (FMOHN, 2023). In another development, it is also one of the six countries contributing 60% of the 10.4 million new cases in the world and one of the fifth countries accounted for over 60% gap between estimated number of incident DR-TB cases and enrolment (Mohammad *et al.*, 2021b). In 2015, two (2) meta-analysis of the prevalence of drug resistant TB in Nigeria shows that, 6% and 32% of newly and previously treated TB cases respectively had MDR-TB. Mycobacterium tuberculosis / Rifampicin resistant assay was endorsed by the WHO in 2010 (Creswell *et al.*, 2014; Van Rie *et al.*, 2010; Geleta *et al.*, 2018). It serves as a platform for the integration of TB and HIV activities in high burdened TB and HIV settings (Narasimooloo and Ross, 2018). The Xpert MTB/RIF assay is a point of care PCR diagnostic method that can identify the DNA of *Mycobacterium tuberculosis* (MTB) and rifampicin resistance. It has high sensitivity and specificity of 97.6% and 99.8% respectively (Mohammad *et al.*, 2020). Therefore, the prevalence and factors associated of drug-resistant tuberculosis among presumptive tuberculosis patients in the study area were determined.

MATERIALS AND METHODS

The research work was conducted in Katsina State, Nigeria. Katsina is one of the States in North West, Nigeria with over 5 million residents projected population. Nigeria has the sixth highest number of tuberculosis cases in the world (NTBLCP, 2023). This study is a retrospective laboratory based study conducted on fourteen (14) Genexpert sites in the States, on presumptive tuberculosis patients that showed clinical signs and symptoms of tuberculosis attending DOTS clinics; within a period of twelve (12) months. Ethical approval to carry out this study was obtained from ethics committee of Katsina State Ministry of Health, Katsina, Nigeria; (certificate number:

MOH/ADM/SUB/1152/1/208), this study was performed in accordance with declaration of Helsinki. Socio-demographic data and other factors associated with drug-resistant tuberculosis were obtained from laboratory registers in the study area.

The results of 14,501 patients were collected and analyzed between January, 2018 and December, 2018; using Chi-Square and odd ratio. MTB/RIF assay (PCR test) was used (Cepheid, Sunnyvale, California USA), as shown in Figure 1, the tests were runned for the period of 1 hour 15 minutes; the results were printed automatically.

RESULTS AND DISCUSSION

Drug-resistant tuberculosis is in existence in the study area, with prevalence of 10.0% among presumptive tuberculosis patients. This finding is higher than the one reported by WHO in 2017, reported 4.3% MDR-TB cases estimated for Nigeria; this could be as a results of samples size. It is also higher than that of Mohammed Yusuf unpublished article whose findings was 3.3% DR-TB among presumptive TB patients in Yobe State, North Eastern, Nigeria; this could also associated with small number of the samples in his study. The study conducted by Mohammad *et al.* (2017) reported 3.1% among presumptive TB patient in Kano, North West, Nigeria; this could be because of small sample size. Davies-Bolorunduro *et al.* (2020) reported DR-TB prevalence of 5.9% in Lagos and its environs. This difference in the prevalence could be attributed to the number of samples analyzed in this studies compare to the number of samples analyzed and reported from Lagos State despite the number GeneXpert machines in Lagos State, they indicated that Lagos State had 30 GeneXpert machines while Katsina has 6 as such this variation in number of facilities could explain the difference in the rate of prevalence (NTBLCP, 2018), if a one year retrospective study is reported in Lagos State, the prevalence could have been higher than ours. This study revealed that males had higher DR-TB prevalence than females 30 (0.15%) and 5 (0.05%); this observation is consistent with WHO (2019) report that TB affects people of both sexes in all age groups but the highest burden is in men. The gender difference in the prevalence of DR-TB in the study area could be related to culture and tradition. In an earlier study, poor health seeking behavior among men, social stigma and cultural habits were adduced for the high prevalence of DR-TB among men (Willeke and Qian, 2015). Studies from Mohammad *et al.* (2021a) in Kano North West, Nigeria and Southern part of Nigeria and other part of Africa showed that the prevalence of DR-TB was significantly high among males.

Beside gender, age group and marital status are some of demographic factors that were found to be significantly associated with DR-TB prevalence in the study area. Findings from Mohammed *et al.* (2023) in Yobe State,

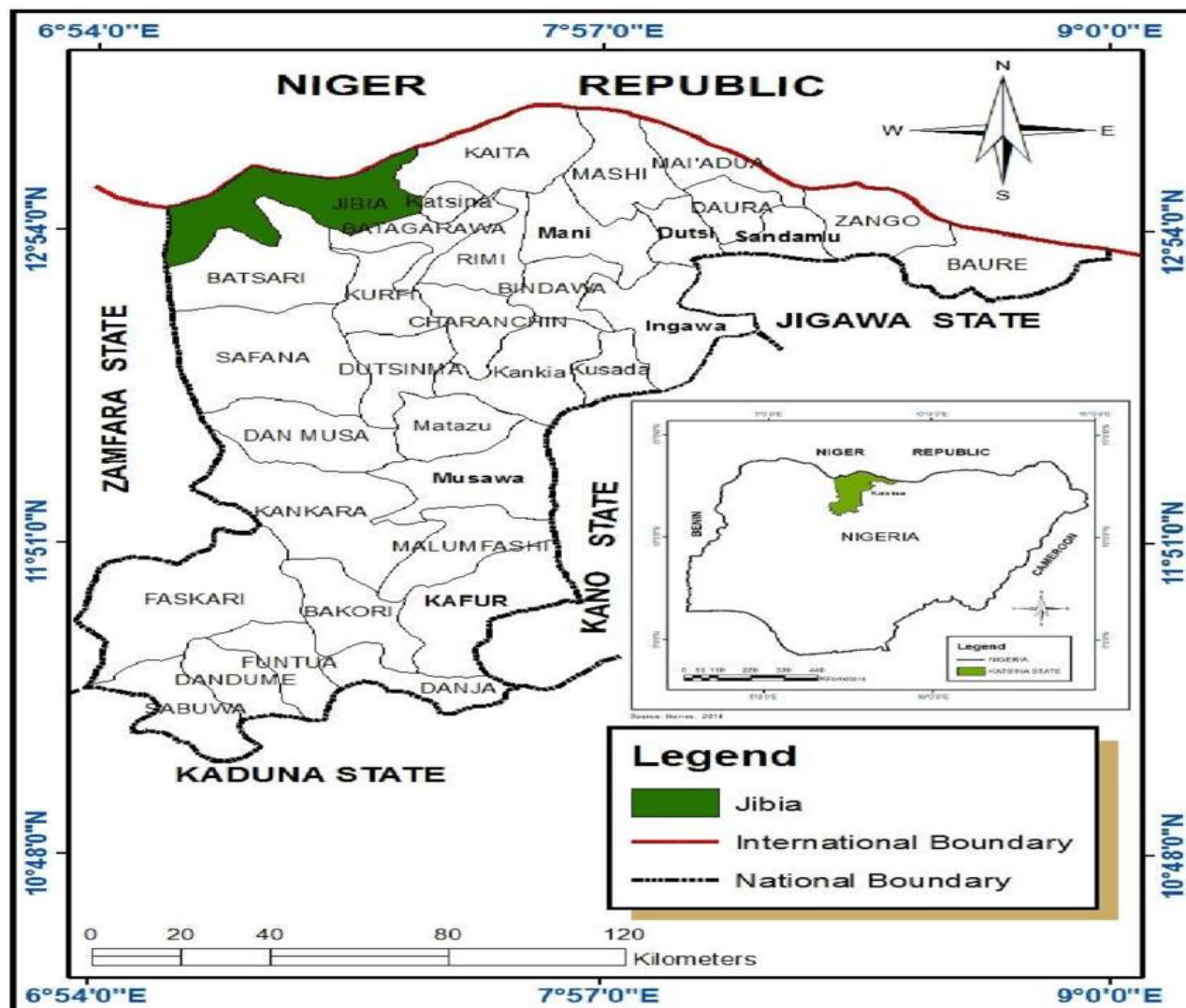


Figure 1. Map of Katsina State (FMOHN, 2023).

North East, Nigeria unpublished article and that of Mohammad *et al.* (2021b), Kano State North West, Nigeria, revealed that patient aged greater than 15 years and those that are married had higher prevalence of DR-TB. The findings of this study are in agreement with WHO (2019), Mohammad *et al.* (2017) and Mohammad *et al.* (2021a) opined that this may not be unconnected with fact that patients in this age group are physically active and may be engaged in various sectors of life working experiences as such becoming more exposed to acquire and develop TB.

In a related study Adejumo *et al.* (2019) in Ibadan South West, Nigeria, identified contact with TB patient among other factors as significant potential in transmission of TB. In an earlier study by Adejumo *et al.* (2019) in Ilorin, North central, Nigeria; revealed that, overcrowding, poor nutrition, poor hygiene and ventilation are some of the factors that promote tuberculosis. The observation of this

study also agrees with the previous studies conducted by Bai *et al.* (2006); FMOHN, (2023); reported that, cigarette smoking is associated with lung infections, predisposing the smoker to tuberculosis infections of all forms. The findings of this study further indicated that, the prevalence of DR-TB is significantly associated with HIV infection because in a study, Mohammad *et al.* (2020) explained that the effect of HIV as witnessed among the TB patients reduces the body peripheral lymphocytes especially CD₄⁺ cells which its depletion can lead to increase in the acquisition and transmission of TB. Reviewed literature indicated that diabetes mellitus is one of the important non communicable disease associated with TB. Result of meta-analysis revealed that 15% of TB patients in Nigeria are having diabetes (FMOHN, 2023). The observation in this study indicated that the prevalence of DR-TB is significantly associated with diabetes as patients with this condition had significantly higher DR-TB prevalence

Table 1. Socio-demographic characteristics and other risk factors associated with Drug resistant tuberculosis (n=14,501).

Socio-demographic Factors	No of Respondents	Percentage (%) prevalence	X ²	Df	p-value
Gender					
Male	7,640	30 (0.2)	1.767	1	0.184
Female	6,861	5 (0.03)			
Total	14,501	35 (0.2)			
Age Group					
≤15 years	906	0 (0.0)	3.327	5	0.650
>15 years	5955	35 (0.2)			
Total	14,501	35 (0.2)			
Marital status					
Married	5455	7 (1.8)	13.653	2	*0.000
Unmarried	9,046	5 (1.3)			
Total	14,501	35 (3.1)			
Occupational status					
Employed	560	6 (0.04)	1.119	3	0.772
Un-employed	13,941	29 (0.16)			
Total	14,501	35 (0.2)			
Educational status					
Formal education	7,981	7 (0.05)	4.032	3	0.258
Non formal education	6520	28 (0.19)			
Total	14,501	35 (0.2)			
HIV Status					
Positive	1102	6 (0.04)	24.219	2	*0.000
Negative	8709	21 (0.14)			
Unknown	30	8 (0.1)			
Total	14,501	35 (0.2)			
Smoking					
Yes	1505	15 (0.10)	14.204	1	*0.006
No	12,996	20 (0.14)			
Total	14,501	35 (0.2)			
Contact with TB Patient					
Yes	3205	12 (0.08)	9.658	1	*0.002
No	374	23 (0.12)			
Total	14,501	35 (0.2)			
Alcohol consumption					
Yes	115	2 (0.01)	0.163	1	0.686
No	14,501	33 (0.19)			
Total	384	35 (0.2)			

*Statistically significant.

compared to TB patients without diabetes.

A systematic review of the prevalence of DR-TB in Nigeria showed that the prevalence of DR-TB in the country varied across geographical regions, settings and the methods used (Van Rie *et al.*, 2010). The higher prevalence obtained in this study may be due to the study setting and large sample size, DOTS clinics in the hospitals used serve as a referral clinics for TB and DR-TB in Nigeria. Presumptive DR-TB patients were referred from other hospitals where there is no GeneXpert site to the hospital that has GeneXpert in the state for Xpert MTB/RIF assay. Xpert MTB/RIF assay which was initially limited to patients with TB/HIV co-infection, symptomatic contact of DR-TB adults and previously treated drug sensitive TB patients. However, later the National Tuberculosis and Leprosy Control programme (NTBLCP) (Mohammad *et al.*, 2021b) recommended it for all presumptive TB patients. DR-TB acquisition or emergence status gave 8.3%, 2.3% and 3.8% for HIV positive, HIV negative and those with unknown status, respectively. High rates of DR-TB have been recorded for persons with HIV/PTB co-infection in the study, which is in consonance with the record reported in Brazil, USA and Ethiopia (Willeke and Qian, 2015). Findings from systematic review on the prevalence of DR-TB in Nigeria and Ethiopia (Van Rie *et al.*, 2010) have shown that the current WHO estimate for new and previously treated TB patients for both countries were low which is proof that the burden of DR-TB in Nigeria and other high TB burden countries in Africa is probably higher than the one anticipated in this study (Adejumo *et al.*, 2018).

Many studies have demonstrated that history of previous TB treatment is a strong risk factor for MDR-TB. This could be due to poor attitude of patients towards following the treatment guidelines for anti-TB drugs, and poor management of drug sensitive TB. A survey which analyzed data from 11 countries indicated that the chance of developing resistant TB increased with the length of time of exposure to anti-TB drugs (FMOHN, 2023). Before the introduction of Xpert MTB/RIF assay, the NTBLCP recommended the addition of streptomycin to the anti-TB regimens this prolonged the exposure and consequence resistance to anti-TB drugs.

In this study, the chance of developing DR-TB was higher among patients with symptomatic contact with a known DR-TB patient than those without contact. This finding underscores the continual spread of DR-TB in the community mostly due to failure to promptly diagnose presumptive DR-TB patient and initiation of early treatment. A WHO report showed that of the 1,241 MDR/RR-TB cases diagnosed in 2015, about 50% were enrolled for treatment. In addition, Nigeria is one of the five countries responsible for over 60% gap between incident MDR/RR-TB cases and treatment enrolment (Adejumo *et al.*, 2018). The association between age and MDR-TB is not consistent. While studies from Nigeria, South Africa and Ethiopia have demonstrated a higher prevalence of DR-TB in the lower age groups, another Nigerian study

showed no significant difference between age and DR-TB. The population structure of the study settings may account for the inconsistent findings. However, surveillance data from Central and Eastern Europe have shown that prevalence of MDR-TB peaks in young adulthood (WHO, 2019). There was no gender difference in the prevalence of DR-TB in this study similar to what was reported from other Nigerian studies (Mohammad *et al.*, 2020).

Reviewed literature indicated that diabetes mellitus is one of the important non communicable disease associated with TB. Result of meta-analysis revealed that 15% of TB patients in Nigeria are having diabetes (Davies-Bolorunduro *et al.*, 2020).

Conclusion and Recommendation

This study confirmed the presence of rifampicin resistant TB in the study area; this remains a major public health issue. Therefore, there is need to introduce routine screening of presumptive TB patients in all the local government areas in the state and the services should be available, affordable, and accessible to the patients who need them.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

- Adejumo, O. A., Olusola-Faleye, B., Adepoju, V., Bowale, A., Adesola, S., Falana, A., Owuna, H., Otemuyiwa, K., Oladega, S., & Adegboye, O. (2018). Prevalence of rifampicin resistant tuberculosis and associated factors among presumptive tuberculosis patients in a secondary referral hospital in Lagos Nigeria. *African Health Sciences*, 18(3), 472-478.
- Creswell, J., Codlin, A. J., Andre, E., Micek, M. A., Bedru, A., Carter, E. J., Yadav, R. P., Mosneaga, A., Rai, B., Banu, S., & Ditiu, L. (2014). Results from early programmatic implementation of Xpert MTB/RIF testing in nine countries. *BMC infectious diseases*, 14, 1-12.
- Davies-Bolorunduro, O. F., Nduaga, S. J., Abiodun, A. T., Amuda, B. O., Osulale, K. A., Atoe, K., & Cadmus, S. (2020). Prevalence of rifampicin resistance among presumptive pulmonary tuberculosis patients within lagos and its environs in South-Western Nigeria. *Nigerian Journal of Microbiology*, 34(1), 5188-96.
- Federal ministry of Health Nigeria (FMOHN), (2023). National mid-term up-date presented at Quarterly held at Abuja, Nigeria; Dated 2nd – 4th May, 2023.

- Geleta, D. A., Megerssa, Y. C., Gudeta, A. N., Akalu, G. T., Debele, M. T., & Tulu, K. D. (2015). Xpert MTB/RIF assay for diagnosis of pulmonary tuberculosis in sputum specimens in remote health care facility. *BMC microbiology*, *15*, 1-6.
- International Union Against Tuberculosis and Lung Disease (IUATLD) (2018). Campaign for access to essential medicines. DR-TB drugs under the microscope: sources and prices for drug-resistant tuberculosis medicines. International Union Against Tuberculosis and Lung Disease.
- Mohammad, A. B., Ibrahim, A., Maifada, A. I., Balogun, M. S., Mohammed, Y., Fagge, H. S., Iliya, S., Ibrahim, A. A., & Mukhtar, M. D. (2021a). Prevalence and Factors associated with rifampicin resistance among patients with pulmonary tuberculosis in Kano State, Nigeria. *Nigerian Journal of Microbiology*, *35*(1) 5460-5466.
- Mohammad, A. B., Iliyasu, G., & Habib, A. G. (2017). Prevalence and genetic determinant of drug-resistant tuberculosis among patients completing intensive phase of treatment in a Tertiary Referral Center in Nigeria. *The International Journal of Mycobacteriology*, *6*(1), 47-51.
- Mohammad, A. B., Usman, A. D., Aminu, A. I., Yakubu, A., Magashi, A. M., Mukhtar, M. D., Kawo, A. H., Iliya, S., Hauwa, Y., Gwarzo, F. S., Abdulkadir, A., Sheshe, A. A., & Taura, D. W. (2020). Molecular diagnosis of urinary *Mycobacterium tuberculosis* among patients attending Urology Clinic in Aminu Kano Teaching Hospital, Kano, Nigeria. *Bayero Journal of Medical Laboratory Science*, *5*(2), 11-17.
- Mohammad, A. B., Zakari, F., Yusuf, A. S., Sani, N. M., Wwarzo, A. M., Iliya, S., Gwarzo, F. S., & Mukhtar, M. D. (2021b). Molecular studies on extra-pulmonary tuberculosis among patients attending Aminu Kano Teaching Hospital, Kano, Kano State, Nigeria. *Dutse Journal of Pure and Applied Sciences*, *7*(4a), 1-10
- Muhammed, Y., Sani, N. M., Mienda, B. S., Qossim, M., Sadiq, A. A., & Mohammad, A. B. (2023). Impact of socio-demographic factors on prevalence of rifampicin resistance among patients attending some hospitals in Yobe state of Nigeria. *International Journal of Science and Technology Research Archive*, *5*(1), 14-21
- Narasimooloo, R., & Ross, A. (2012). Delay in commencing treatment for MDR TB at a specialised TB treatment centre in KwaZulu-Natal. *South African Medical Journal*, *102*(6), 360-362.
- National Tuberculosis and Leprosy Control Programme (NTBLCP) (2018). Report on tuberculosis and multidrug resistant tuberculosis diagnosis, treatment and management in Nigeria. National Tuberculosis and Leprosy Control Programme.
- Van Rie, A., Page-Shipp, L., Scott, L., Sanne, I., & Stevens, W. (2010). Xpert® MTB/RIF for point-of-care diagnosis of TB in high-HIV burden, resource-limited countries: hype or hope? *Expert Review of Molecular Diagnostics*, *10*(7), 937-946.
- Willeke, K., & Qian, Y. (1998). Tuberculosis control through respirator wear: performance of national Institute for occupational safety and health-regulated respirators. *American Journal of Infection Control*, *26*(2), 139-142.
- World Health Organization (WHO) (2012). Epidemiology. *Global tuberculosis control: Epidemiology, strategy, financing*. Pp. 6-33.
- World Health Organization (WHO) (2013). *Multidrug and extensively drug-resistant TB (M/XDR-TB): 2013 global report on surveillance and response*. Report no. WHO/HTM/TB/2013.3.
- World Health Organization (WHO) (2019). Anti-tuberculosis Drug Resistance in the World. Report No.4. Prepublication version. Retrieved 5 May 2019 from whqlibdoc.who.int/hq/2018/WHO_HTM_TB_2018.394_eng.pdf.
- World Health Organization Library Cataloguing-in-Publication Data Global tuberculosis report (2014). 1. Tuberculosis – epidemiology. 2. Tuberculosis, Pulmonary – prevention and control. 3. Tuberculosis – economics. 4. Tuberculosis, Multidrug-Resistant. 5. Annual Reports. I. World Health Organization. ISBN 978 92 4 156480 9 (NLM classification: WF 300).
- World Health Organization (WHO) (2014). library cataloguing-in-publication data global tuberculosis report (2014). Tuberculosis epidemiology. Tuberculosis pulmonary-prevention and control. Tuberculosis economics. Tuberculosis, Multidrug-Resistant. Annual Reports. World Health Organization. ISBN 978 92 4 156480 9 (NLM classification: WF 300).