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Low Detection Rate of Multidrug-Resistant and Rifampicin-Resistant Tuberculosis in the Democratic Republic of Congo: Trend Analysis 2013-2017

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Abstract

The Democratic Republic of Congo is one of the countries with a high prevalence of multidrug-resistant tuberculosis (MDR-TB) in Africa and worldwide. This study aims to describe the trends and level of screening since 2013. This is a retrospective descriptive study based on quarterly reports from the provinces. The number of cases, past histories, age, sex and HIV Co-infection was identified. It emerges that the number of cases increases significantly but does not reach the forecasts yet (912 cases of MDR/RR and XDR diagnosed in 2017 out of 3948 cases expected with a gap of 77%). Patients with a history of TB predominate (63.5% in 2017); but the proportion of patients with no history of TB increases (36.5% in 2017). This suggests high rates among contacts. Women (37.8%) and children under 15 (2.7%) are less represented. TB/HIV Co-infection is 12% as for sensitive cases. Efforts still need to be made to improve screening.

Keywords

MDR-RR TB, Trends Screening, DRC

1. Introduction

Drug resistance to first- and second-line TB drugs represents a major challenge for overall control of TB [1] [2] [3] [4]. For 2015, the World Health Organization (WHO) estimated that 480,000 new cases of tuberculosis and approximately 14% of previously treated cases had drug-resistant TB strains; only 132,120 cases

were reported [2]. The best estimate is that, worldwide in 2017, 558,000 patients (range 483,000 - 639,000) developed TB that was resistant to Rifampicin (RR-TB) and of these, 82% had multi-resistant TB form (MDR-TB) with resistance to at least Rifampicin and Isoniazid [5]. The exact estimate of the incidence of this infection remains difficult because of variations in strategies and reporting across different countries. But three countries accounted for almost half of the world's cases of MDR/RR-TB: India (24%), China (13%), Russian Federation (10%) [3] [5]. Globally, 3.5% of new TB cases and 18% of previously treated cases had MDR/RR-TB in 2017 [3]. Among cases of MDR/RR-TB, 8.5% were estimated to have extensively drug-resistant TB (XDR), in which there is also associated fluoroquinolone and/or second-line injectables (kanamycin, amykacin, capreomycin) resistance [3].

The Democratic Republic of Congo (DRC) is one of 30 countries that bear the burden of TB in the world; it is among the 27 leading countries for the drug-resistant form and the top 4 in Africa with South Africa, Nigeria and Ethiopia [5]. The National resistance survey conducted in 2015 showed that 2.17% of new cases of pulmonary tuberculosis and 15.82% of retreatment cases were resistant to rifampicin and isoniazid [6]. Annual statements are far from WHO projections. This study seeks to describe trends in detection of RR/TB and MDR-TB in DRC between 2013 and 2017. At this period, the country began a new strategy with implementation of Gene Xpert equipment (Xpert MTB/RIF, Cepheid, USA) in all the 26 provinces. The main purpose is to contribute to the control of the disease in a context of limited resources.

2. Material and Method

This is a descriptive retrospective study. It is based on provincial quarterly reports validated during the annual reviews of the National Tuberculosis Program (NTP) for the period 2013-2017. The data concern children and adults. The concepts used meet WHO definitions [5]. The term "Multidrug Resistant" (MDR) applies to patients with at least rifampicin and isoniazid resistance without the combination of quinolones or injectables [5]. Cases with isolated resistance to rifampicin (RR) without isoniazid are also reported as such because they are more likely to be MDR. Extensively Resistant Tuberculosis cases (XDR) are not reported.

As a strategy, samples from the alleged MDR [1] [4] [7] [8] are tested on GeneXpert (Xpert MTB/RIF, Cepheid.USA). The country has 84 sites with GeneXpert. Specimens with resistance to rifampicin are subjected to the Line Probe Assay (LPA-MTBDRplus-sl or Hain test) to test other molecules: Isoniazid, Fluoro-quinolone, injectables and thus exclude XDR tuberculosis. All samples are also sent for performing Löwenstein-Jensen culture. There are 2 sites with LPA and an operational laboratory for culture for the whole country.

Variables studied are: age, sex, HIV state, previous TB treatment, origin (province).

The quarterly reports were collected by the Central data manager of the NTP. At this level annual synthesis is performed.

The descriptive statistics consisted of calculating the mean and standard deviation for the quantitative data and proportions (percentages) for the categorical data.

3. Results

1) Trend in the Screening of Multidrug-Resistant and Rifampicin-Resistant TB cases in Democratic Republic of Congo 2013-2017

Table 1 presents results by year compared to all cases of tuberculosis detected.

Overall, the number of tuberculosis cases detected has increased by 38%. For drug-resistant forms, this is also influenced by the increase in the number of GeneXpert equipment across the country from 2013. In the past, only two provinces had the equipment (Kinshasa, South Kivu). Actually all the 26 provinces are covered.

2) Provincial grouping based on the number of cases detected in 2017:

In 2017, four provinces report 72% of MDR/RR-TB cases in the country: Kinshasa (32%), Haut Katanga (15%), Kongo Central (13%), Kasai Oriental (12%). The other 22 provinces share 28%. The 4 provinces are considered as "Hot Spots" for drug-resistant TB. Figure 1 shows the prevalence by province.

3) Patients with MDR/RR -TB by Gender in DRC: 2013-2017:

Table 2 gives the distribution of MDR/RR-TB patients by sex and year. Women are fewer. The sex ratio (M:F) is 1.6:1.

4) Patients with MDR/RR-TB by age:

Mean-age is 35.5 (11.3) years. Eighty-two patients are aged 0 to 14 years (2.7%). The group aged 15 years or more is predominant.

5) Previous history of tuberculosis

Patients with a history of tuberculosis predominate. However, the number of those without a history of tuberculosis is increasing substantially to double 2013 in 2017. Table 3 summarizes the data.

6) Co-infection TB-VIH

Analysis is based on 2017 data only. From 893 cases screened, 518 (58%) were tested for HIV, 61 (12%) were HIV positive. HIV testing depended on the availability of the device and reagents in the health facilities.

Table 1. Cases of MDR-TB and RR-TB in DRC: 2013-2017.

Year	Total TB Cases (n)	TB-MDR (n)	TB RR (n)
2013	110,563	334	41
2014	117,681	424	32
2015	121,024	466	40
2016	133,262	646	63
2017	152,744	803	90
TOTAL	635,274	2673	266

Table 2. MDR /RR-TB in DRCongo by sexe: 2013-2017.

Year	Total Cases (n)	Male (n)	%	Female (n)	%
2013	375	213	56.8	162	43.2
2014	456	284	62.3	172	37.7
2015	506	341	67.4	165	32.6
2016	709	434	61.2	275	38.8
2017	893	555	62.1	338	36.9
Total	2939	1827	62.2	1112	37.8

Table 3. History of TB in MDR and RR Patients 2013-2017.

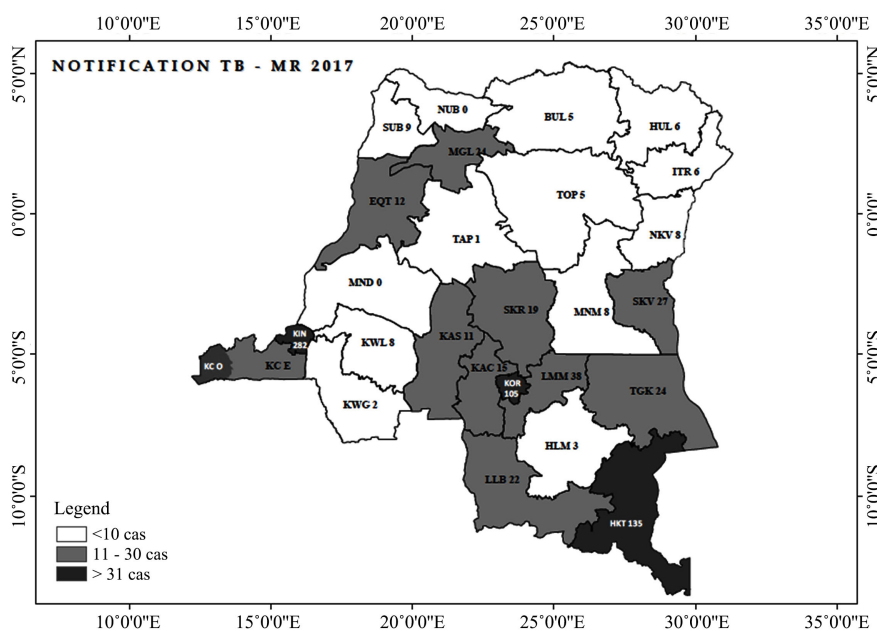| Year	Total Cases (n)	No TB History		TB History	
		n	%	N	%
2013	375	55	14.7	320	85.3
2014	456	90	19.7	366	80.3
2015	506	110	21.7	396	78.3
2016	709	126	17.8	583	82.2
2017	893	326	36.5	567	63.5
TOTAL	2939	707	24.0	2232	75.9

Figure 1. Prevalence of TB-MDR/RR in DR Congo by province. SUB = Sud Ubangi, NUB = Nord Ubangi, BUL = Bas Uélé, HUL = Haut Uélé, ITR = Iturie, EQT = Equateur, MGL = Mongala, TOP = Tshopo, NKV = Nord Kivu, TAP = Tshwapa, MND = Mai-Ndombe, KAS = Kasai, KAC = Kasai Central, SKR = Sankuru, KOR = Kasai Oriental, HLM = Haut Lomami, MNM = Maniema, SKV = Sud-Kivu, TGK = Tanganika, HKT = Haut Katanga, LLB = Lualaba, KWL = Kwuilu, KWG = Kwango, KCE = Kongo Central Est, KCO = Kongo Central Ouest, KIN = Kinshasa, LMM = Lomami. The 4 Hot-Spot provinces are highlighted in black: Kinshasa, Kongo Central, Kasai Central and Haut Katanga.

4. Discussion

DR Congo is among the 30 countries worldwide bearing the burden of the TB as endemic [2] [4] [5]. Drug-resistant forms are increasingly being detected. We have observed an increase in cases for both susceptible and drug-resistant TB between 2013 and 2017. This trend is expected to continue if we consider the expected prevalence of 250 cases of Tuberculosis/all forms per 100,000 inhabitants [4]. The current progress is based on initiatives such as The Global Fund for Tuberculosis, Malaria and HIV, Damien Action, Challenge TB etc.

However, the number achieved remains below the WHO estimates [7]. In 2017, there were 893 cases of MDR-RR TB and 19 XDR; that was below the expected number of 3948 cases [5]. The national survey on TB drug resistance conducted in 2015 found a prevalence of 2.17% among new cases and 15.82% for retreatment cases [6]. This rate remains lower than those described in other countries such as Angola and Ethiopia, where 8% and 4.1% are respectively reported in the group of new cases, and 71.1% and 19% respectively cases already treated for tuberculosis [9] [10] [11] [12] [13]. Urgent action is required to improve the coverage and the quality of diagnosis and treatment for people suspected to be infected by resistant TB strains. Closing gaps in detection and treatment requires much higher coverage of drug susceptibility testing among TB patients, reducing underdiagnosis of TB, improving access on new diagnosis tools and better organization of health system [8] [14].

MDR/RR TB patients with a history of tuberculosis account for two-thirds. This is usual. Results reported in other countries are similar [9] [12] [15] [16]. It should be noted, however, that there is an increase in the number of patients without a history of tuberculosis that can reflect the importance of contacts. Strengthening the strategy for mapping contacts is advised.

Four provinces screen 72% of MDR-RR TB cases in the country. They are considered as Hot Spots for drug-resistant TB. Two have areas with intense mining activities. For the 2 others, it is a big city and a harbor with intense activity. This context requires innovative approaches to manage particular patients such as mine workers, harbor residents and crowded cities with often comorbidities [17].

Women are fewer. This is seen even for sensitive TB. Marçôa D. *et al.* report a sex ratio of 1.6:1 for men [18]. On the one hand, they mention the difficulties women in resource-poor countries face in accessing health facilities. On the other hand, men have comorbidities that may expose them to tuberculosis and phamaco-resistant forms; include alcohol, tobacco, imprisonment, and HIV. In women, the overall prevalence of tuberculosis reported remains lower than in men and this has been reported for many infectious diseases. Interactions between sex hormones and the immune system are thought to be implied in the differences observed.

Patients younger than 15 years represent only 2.7%. Overall, children are less numerous for both sensitive TB and drug-resistant forms [4] [5]. Several factors

challenge confirmation of TB among children: low bacillary load, difficulty coughing, and high frequency of extra-pulmonary forms requiring more specialized investigations [17]. Algorithms are available but they require capacity building for the staff providing care.

Co-infection with HIV is found in 12% of patients in this study. This percentage is similar to that found in sensitive TB cases [19]. Although HIV infection is recognized as a potent risk factor for developing TB in a person with latent TB, it is not formally recognized as risk factor for the development of drug-resistant TB. [17] Person living with HIV will develop both sensitive and resistant TB. However, during treatment with ARVs, some adverse effects may alter the absorption of antituberculosis drugs or lead to dysfunction that may lead to drug resistance.

5. Conclusion

The detection of MDR/RR TB cases in DRC has been increasing since 2013. However, the gap to be covered compared to projections remains high. This can be explained by the difficult access to diagnostic sites. The small number of women and children requires an appropriate approach in the epidemiological context. Strengthening teams to identify suspects, supporting the dispatch network of samples from health centers to diagnostic laboratories and increasing the number of laboratories for performing culture and LPA will significantly improve screening.

Limitations of This Study

As retrospective study, it was not easy to have information about contacts tracking and so answer the progressing rate of new cases among MDR/RR TB diagnosed. Also, the feedback from the main laboratories to the health structures was not always given to certify the results. These aspects will be corrected by a cohort study now undergoing.

Authors Contributions

Innocent Kashongwe Murhula: Conception, data organization and manuscript management;
Fina Mawete: collection of data from national MDR/ RR and XDR TB reports, manuscript management;
Lay Ofali: data collection from TB susceptible report;
Michel Kaswa: Supervision of data collection;
Francois Lepira Bompeka: reviewer of manuscript;
Jean Marie Kayembe Ntumba: Manuscript Management;
Zacharie Kashongwe Munogolo: Coordination of study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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