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REVIEW

Epidemiology and genetic diversity of multidrug-resistant tuberculosis in East Africa

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SUMMARY

Multidrug-resistant tuberculosis (MDR-TB) is an emerging problem in many parts of the world, and levels of MDR-TB among new TB patients are increasing in sub-Saharan Africa. We reviewed the prevalence and molecular epidemiology of MDR-TB in East Africa, including Burundi, Kenya, Rwanda, Tanzania, and Uganda. In 16 epidemiologic surveys, the prevalence of MDR among new cases ranges from 0.4% in Tanzania to 4.4% in Uganda, and among recurrent cases ranges from 3.9% in Tanzania to 17.7% in Uganda. There is a gap of 5948 cases between the estimated number of MDR-TB cases in East Africa and the number actually diagnosed. The only confirmed risk factors for MDR-TB are prior treatment for TB and refugee status. HIV has not been reported as a risk factor, and there are no reports of statistical association between spoligotype and drug resistance pattern. Increased capacity for diagnosis and treatment of MDR-TB is needed, with an emphasis on recurrent TB cases and refugees.

1. Introduction

Multidrug-resistant tuberculosis (MDR-TB), defined as disease caused by *Mycobacterium tuberculosis* resistant to at least isoniazid and rifampicin, is an emerging problem in many parts of the world. In 2011, there were an estimated 630,000 cases of MDR-TB among the world's 12.0 million prevalent cases of TB [1]. The WHO estimates that levels of MDR-TB among new TB patients are increasing in Africa. However, the prevalence, epidemiology, genetic mutations conferring drug resistance and genetic diversity of MDR-TB vary across the continent. Here we review the prevalence and molecular epidemiology of MDR-TB in East Africa.

The East African Community (EAC) was created in 2001 as a free trade union between the countries (population in million) of Burundi (9), Kenya (42), Rwanda (11), Tanzania (46), and Uganda (35) [1,2]. The mission of the EAC is to create economic prosperity and political security across the region. The establishment of a free trade and customs union has made these five nations politically and economically intertwined. The inter-dependence between the nations facilitates trade, travel, and migration, creating the potential for the spread of MDR-TB between the nations. Currently, Kenya, Uganda and Tanzania are among the 22 high TB burden countries worldwide. None of the EAC countries are among the 27 high MDR-TB burden countries; however, recent MDR-TB outbreaks in South Africa demonstrate the importance of surveillance and vigilance [3].

Therefore, this review examines the prevalence, case detection and treatment rates, risk factors, profile of mutations conferring multidrug-resistance, and genotypic diversity of MDR-TB in East Africa.

2. Methods

2.1. Study design

We conducted a systematic literature review for original articles published in English focusing solely on data from January 1997 through the end of December 2012.

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2.2. Search strategy

We performed a systematic search of online databases including PubMed/Medline, Embase, Popline, Global Health, Google and Web of Knowledge. We used the search terms beginning with the text string 'tuberculosis' in all possible combinations with 'multidrug resistance', 'drug resistance', 'MDR', and other related keywords including 'genotypes', 'spoligotypes', 'prevalence', 'HIV', 'HIV/AIDS' and 'diagnosis'. Each term was searched separately with the text string 'East Africa' and then with the name of the specific country in East Africa region. Case reports were included. We also reviewed the WHO websites for relevant publications. New links displayed beside the abstracts were followed and retrieved. Finally, the bibliographies of each article were carefully reviewed and relevant articles also retrieved.

2.3. Inclusion and exclusion criteria

We screened titles and abstracts for relevance, and subsequently reviewed the full texts of manuscripts that were potentially pertinent. Only study reports that used original data and had evaluated multidrug-resistant tuberculosis in East Africa were included.

2.4. Data extraction and analysis

Eligible studies were reviewed independently by two authors (BRK and LEW). Due to heterogeneity in study reporting, a structured form for data extraction was created that included: i) exact site and country where the study was conducted; ii) study year and duration; iii) year of publication; iii) study population and setting; iv) number of TB patients recruited; v) type of TB patients involved (new or previously treated cases); vi) procedure for recruitment; vii) study outcome(s) of interest (prevalence of MDR-TB, prevalence of rifampicin resistance, types of mutations conferring resistance, spoligotypes and risk factors for MDR-TB). Extracted data were entered into a Microsoft Excel spreadsheet (Microsoft, Redwoods, WA, USA) for analysis using STATA version 12 (StataCorp LP, College Station, TX, USA). Results were expressed as percentages.

3. Results and discussion

3.1. Reported and estimated incidence of MDR-TB in East Africa

The total number of TB cases and MDR-TB cases identified in each country of the EAC between 2005 and 2011 is summarized in Table 1. As a proportion of total tuberculosis cases reported, the number of confirmed MDR cases ranged from 6/6828 (0.09%) in Burundi to 76/6784 (1.12%) in Rwanda. Additionally, there have been 16 published surveillance studies from East Africa with a well defined patient enrollment criteria reporting levels of MDR-TB; these studies are detailed in Table 2 [4–19]. Levels of MDR among new TB patients in the independent surveillance studies ranged from 0.4% in Tanzania to 4.4% in Uganda [10,15]. Levels of MDR among recurrent TB cases ranged from 3.9% in Tanzania to 17.7% in a Uganda [13,19]. Based upon the reported cases and surveillance data, the World Health Organization (WHO) estimated the MDR-TB burden of all new and retreatment cases in 2011 for Burundi, Kenya, Rwanda, Tanzania and Uganda ranging from 1.2% in Tanzania to 4.8% in Rwanda (Table 3) [20–24].

3.2. Cases of confirmed MDR-TB and gaps in MDR-TB testing and treatment

There is a large gap between the numbers of estimated cases of MDR and numbers of confirmed cases of MDR-TB in East Africa. Of the 227,759 notified TB cases in East Africa in 2011, the WHO estimated 6331 MDR-TB cases (Table 4) [20–24]. Only 387 cases of MDR-TB were actually confirmed through diagnostic testing in 2011, and therefore nearly 6000 cases of MDR-TB are undiagnosed and untreated in East Africa each year [20–24].

The capacity to diagnose *M. tuberculosis* drug resistance and treat MDR-TB must increase and be considered an essential

Table 1
Epidemiology and number of confirmed MDR-TB cases in East Africa as reported by the WHO: 2005–2011.*

East African country	2005	2006	2007	2008	2009	2010	2011
Burundi							
Population in million	7	8	8	8	8	8	9
TB cases notified	6585	6114	6284	6808	7277	7719	6828
Confirmed MDR-TB cases†	–	0	26	17	0	24	6
% of TB cases that is MDR	–	0	0.41	0.25	0	0.31	0.09
Kenya							
Population in million	36	37	38	39	40	41	42
TB cases notified	102,680	108,342	106,438	99,941	102,997	106,083	103,981
Confirmed MDR-TB cases†	44	89	82	102	150	112	166
% of TB cases that is MDR	0.04	0.08	0.08	0.10	0.15	0.11	0.16
Rwanda							
Population in million	9	9	9	10	10	11	11
TB cases notified	7220	8117	7638	7472	7251	7065	6784
Confirmed MDR-TB cases†	35	–	102	79	78	90	76
% of TB cases that is MDR	0.48	–	1.34	1.06	1.08	1.27	1.12
Tanzania							
Population in million	39	40	41	42	44	45	46
TB cases notified	61,022	59,282	59,371	60,490	71,643	63,453	61,148
Confirmed MDR-TB cases†	10	13	169	24	24	34	68
% of TB cases that is MDR	0.02	0.02	0.28	0.04	0.03	0.05	0.11
Uganda							
Population in million	29	30	31	32	33	33	35
TB cases notified	41,040	40,782	40,909	42,178	41,703	45,546	49,018
Confirmed MDR-TB cases†	46	–	–	26	57	93	71
% of TB cases that is MDR	0.11	–	–	0.06	0.14	0.20	0.14

* These are the numbers of cases confirmed and reported by national tuberculosis (TB) programs to the World Health Organization (WHO) [20–24,49].
† Confirmed multi-drug resistant tuberculosis (MDR-TB) are those newly diagnosed with resistance to at least isoniazid and rifampicin.