OUTCOME OF TREATEMENT OF MULTI-DRUG RESISTANT TUBERCULOSIS PATIENTS IN ABBASIA CHEST HOSPITAL IN 2008-2011

Thesis

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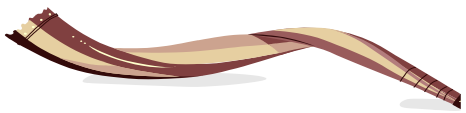

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Introduction

Multidrug-resistant tuberculosis (MDR-TB) is defined as TB that is resistant, at least, to Isoniazid (INH) and Rifampicin (RMP), the two most powerful first-line anti-TB drugs. Isolates that are multiple resistant to any other combination of anti-TB drugs but not to INH and RMP are not classed as MDR-TB ***(M/XDR-TB, 2010).***

MDR-TB most commonly develops in the course of TB treatment and most commonly due to doctors giving inappropriate treatment or patients missing doses or failing to complete their treatment ***(Goble et al., 1993).***

MDR-TB strains are often less fit and less transmissible, and outbreaks occur more readily in people with weakened immune systems (e.g., patients with HIV) ***(Florida and New York, 1991).***

The recommendations encourage the wider use of rapid drug-susceptibility testing with molecular techniques to detect TB patients with Rifampicin resistance and provide adequate treatment. The use of culture remains important for the early detection of failure during treatment. Systems that primarily employ ambulatory models of care to manage patients with drug-resistant TB are recommended over others based mainly on hospitalization. National TB control programs, public health

decision-makers and technical and implementing partners involved in the control of MDR-TB are encouraged to use the recommendations to guide their work, and to adapt national guidelines accordingly. Performing monthly sputum smear microscopy and culture were the best strategy in identifying failures earlier. Sputum smear microscopy alone resulted in delayed detection of failure: when done at monthly rather than two monthly intervals it increased the detection of failure slightly (not significantly). Use of drugs to which the strain was reportedly susceptible showed a marginal benefit when compared with their use regardless of susceptibility patterns. Choice of drug would thus depend on the direct sensitivity test (DST) of the strain isolated from the patient or close contacts with MDR-TB ***(Guidelines for the programmatic management of drug-resistant tuberculosis- update, 2011a).***

Studies showed that the intensive phase should be contain at least four drugs to be effective, as well as pyrazinamide during the intensive phase of treatment. No evidence found to support the use of more than four second-line anti-tuberculosis drugs in patients with extensive disease. Increasing the number of second-line drugs in a regimens permissible if the effectiveness of some of the drugs is uncertain. The regimen should include Pyrazinamide, a Fluoroquinolone, a parenteral agent, Ethionamide (or

Prothionamide), and Cycloserine, or else PAS (Para Amino Salicylic Acid) if Cycloserine cannot be used. Ethambutol may be used but is not included among the drugs making up the standard regimen ***(Guidelines for the programmatic management of drug-resistant tuberculosis-update, 2011b).***

Usually, multidrug-resistant tuberculosis can be cured with long treatment of second-line drugs, but these are more expensive than first-line drugs and have more adverse effects. There is evidence that previous therapy with a drug for more than one month was associated with diminished of that drug regardless of vitro tests indicating susceptibility ***(Globe et al., 1993).***

In the treatment of patients with MDR-TB, an intensive phase of at least 8 months' duration is recommended and total treatment duration of at least 20 months is recommended in patients without any previous MDR-TB treatment. It is not unusual for patients with MDR-TB to be on treatment for two years or more ***(WHO, 2011).***

Aim of the Work

Exploring factors affecting favorable treatment outcome of MDR-TB patients in Abbassia Chest Hospital in 2008-2011.

Epidemiology of TB

Tuberculosis (TB) is a major global health problem. Each year, there are around 9 million new cases of TB, and close to 2 million people die from the disease. All countries are affected, but most cases (85%) occur in Africa (30%) and Asia (55%), with India and China alone accounting for 35% of all cases ***(The global plan to stop TB, 2011-2015).***

There are 22 so called high-burden countries (HBCs) that account for about 80% of the world's TB cases, and which have been given particular attention in TB control since around the year 2000 ***(The global plan to stop TB, 2011-2015).***

Globally, the absolute number of cases is increasing slowly, although the number of cases per capita (usually expressed as the number of cases per 100,000 populations) is falling by around 1% per year. TB ranks as the eighth leading cause of death in low- and middle-income countries (seventh for men and ninth for women); among adults aged 15–59, it ranks as the third cause of death, after HIV/AIDS and ischemic heart disease ***(The global plan to stop TB, 2011-2015).***

The HIV epidemic caused a major upsurge in TB cases in Africa during the 1980s and 1990s, with cases per 100,000 populations growing from less than 200 to more than 350 cases

per 100,000 populations. Numbers peaked in 2004, and have since begun to decline, following trends in the HIV epidemic, but with a time-lag of about six years ***(The global plan to stop TB, 2011-2015).***

Inadequate treatment of MDR-TB can lead to worse patient outcome and more chance for the emergence of extensive drug resistance ***(Mukherjee et al., 2004).***

The case detection rate of positive cases in Egypt was 72% and treatment success rate was 87%. Moreover, Egypt did not stand on this, but keep stepping ahead on the target of disease eradication to achieve 78% case detection and 89% treatment success in 2008. In the year 2003, Egypt applied to the Green Light Committee to establish a DR-TB management project. The plan involved establishing four centers to cover the whole country. The first center was established in Abbassia Chest hospital. The project was approved and patient enrollment started in July 2006 ***(The National Tuberculosis Program of Egypt, 2011a).***

In regular tuberculosis management, Egypt has succeeded to:

a. Achieve the global target (i.e. detecting at least 70% of smear positive cases)

b. Successfully treating at least 85% of the detected cases) and occupying a place in the target zone, as published in

the Global Report of World Health Organization 2009 (which describes the data of 2007). Be classified as one of the 36 worldwide countries that have achieved the global targets in both case detection and treatment success in year 2007.

(The National Tuberculosis Program of Egypt, 2011a)

Global magnitude of the DR-TB problem:

Based on available information from the duration of the Global Project, the most recent data available from 116 countries and settings were weighted by the population in areas surveyed, representing 2,509,545 TB cases, with the following results:

- Global population weighted proportion of resistance among new cases: any resistance 17.0%, Isoniazid resistance 10.3% and MDR-TB 2.9%.
- Global population weighted proportion of resistance among previously treated cases: any resistance 35.0%, Isoniazid resistance 27.7%, MDR-TB 15.3%.
- Global population weighted proportion of resistance among all TB cases: any resistance 20.0%, Isoniazid resistance 13.3% and MDR-TB 5.3%.
- China and India carry approximately 50% of the global burden of MDR-TB and the Russian Federation a further 7%.

(WHO, 2008)

The problem of MDR-TB is further amplified by the emergence of extensively drug resistant TB (XDR-TB) strains, which are strains of MDR-TB resistant as well to any one of the Fluoroquinolones and to at least one of the three injectable second-line drugs (Amikacin, Capreomycin or kanamycin). XDR-TB showed an increased proportion from 5% to 7% of MDR isolates referred to supranational reference laboratories between 2000 and 2004 ***(WHO, 2008a).***

Treatment of multidrug-resistant TB (MDR-TB) of which there is around 0.4–0.5 million cases each year is more challenging. It requires use of second-line drugs (including injectable antibiotics) that are more costly and cause more severe side-effects, and recommended regimens must be taken for up to two years ***(Drug-resistant tuberculosis Emergency update, 2008a)***.

Cure rates for MDR-TB are low, typically ranging from around 50% to 70%. Among people living with HIV, diagnosis of TB can be more difficult compared to those who are HIV-negative, and mortality rates are higher. Just over 10% of the TB cases that occur each year are among people living with HIV, and around 80% of these cases are in Africa (where around one third of TB cases are among people who are HIV-positive)**.** In 2010, there was an estimated prevalence of

650,000 cases of multidrug-resistant TB (MDR-TB), and in 2008 it was estimated there were 150,000 MDR-TB deaths annually. The number of patients enrolled on MDR-TB treatment increased to 46,000 in 2010. While more people are being treated for MDR-TB in 2010, it is just 16% of the estimated number of MDR-TB patients that needed treatment i.e. MDR-TB patients that would be identified if all newly-notified TB patients were tested for drug resistance ***(The National Tuberculosis Program of Egypt, 2011b).***

The MDR-TB problem in EGYPT in 2011 described in table (1).

Table (1): Magnitude of the MDR-TB problem in Egypt 2011

Reported cases of MDR-TB 2011	**New**	**Retreatment**	**Total**
Cases tested for MDR-TB	39 (<1%)	497 (74%)	536
Laboratory-confirmed MDR-TB cases	5	129	134
Patients started on MDR-TB treatment			71(13%)

http://www.who.int/countries/egy/en/

In Egypt, a nationwide drug resistance survey was carried out in 2002, in which a total number of 849 patients enrolled, 632 new and 217 old patients, and showed in table (2).

Table (2): Magnitude of the DR-TB problem in Egypt

Monoresistance	Among new patients	Among retreated patients
Isoniazid INH	2.7%	2.8%
Rifampicin R	3.5%	6.9%
Ethambutol E	0.5%	0.9%
Streptomycin S	15%	7.8%
MDR-TB	Among new patients	Among retreated patients
INH + R	0%	2.3%
INH + R + E	0%	0.9%
INH + R + S	0.8%	9.7%
INH + R + E + S	1.4%	25.3%

(NTP Egypt guidelines, 2011f)

TB Control in Egypt:

In its widest sense tuberculosis (TB) control refers to all aspects of health protection, i.e. prevention of tuberculosis and of its complications; early diagnosis; appropriate treatment; patient information and rehabilitation; and, research in different areas related to tuberculosis ***(WHO, 2009).***

Tuberculosis control consists of a variety of activities carried out by different persons in governmental, non-governmental and private organizations and institutions. These activities include immunization (BCG); case finding and treatment; health education; and, surveillance of the disease in the community ***(WHO, 2009).***

TB control in Egypt dates back to 1926 when a big hospital was established in Helwan (Helwan sanatorium). This was followed by the establishment of two chest dispensaries in 1930. Gradually a network of chest dispensaries and hospitals was set up all over the country. Patients were usually hospitalized for isolation and treatment ***(WHO, 2009).***

The Egyptian National Tuberculosis Control Program (NTP) was launched in 1989. In 1996 the NTP adopted the WHO' DOTS (Directly Observed Treatment with Short Course) strategy and reached nationwide coverage by the year 2000 through involving the primary health care centers (PHCs), which are about 5000 all over the country. The calculated Annual Risk of Infection in the year 2008 was 0.21%.Case detection of new smear positive cases was 72% in 2007 with 87% treatment success rate ***(WHO, 2009).***

Definitions:

Case definitions:

The TB case definitions below are based on the level of certainty of the diagnosis and on whether or not laboratory confirmation is available ***(WHO, 2010a).***

Definition of tuberculosis suspect:

Any person who presents with symptoms or signs suggestive of TB, the most common symptom of pulmonary TB is a productive cough for more than 2 weeks, which may be accompanied by other respiratory symptoms (shortness of breath, chest pains, hemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue) ***(WHO, 2010a).***

Case of tuberculosis:

A definite case of TB is a patient with Mycobacterium tuberculosis complex identified from a clinical specimen, either by culture or by a newer method such as molecular line probe assay. In countries that lack the laboratory capacity to routinely identify *M.* tuberculosis, a pulmonary case with one or more initial sputum smear examinations positive for acid-fast bacilli (AFB) is also considered to be a "definite" case, provided that there is a functional external quality assurance (EQA) system

with blind rechecking ***;***Or one in which a health worker (clinician or other medical practitioner) has diagnosed TB and has decided to treat the patient with a full course of TB treatment ***(www.who.int/tb/dots/laboratory/policy/en/ index1. html).***

N.B.: Any person given treatment for TB should be recorded as a case. Incomplete "trial" TB treatment should not be given as a method of diagnosis ***(WHO, 2010a)***.

Cases of TB are also classified according to the:

- **Site of disease.**
- **Bacteriological results (including drug resistance).**
- **History of previous treatment.**

Each of these key features of TB cases is discussed below:

1) Site of TB disease:

In general, recommended treatment regimens are similar, irrespective of site. Defining the site is important for recording and reporting purposes and to identify the more infectious patients – those with pulmonary involvement {who will be further subdivided by smear status} ***(WHO, 2010a).***