RESISTANCE TO INH AND RIFAMPICIN IN PULMONARY TUBERCULOUS PATIENTS

Thesis Submitted for Partial Fulfillment of Master Degree in Chest Diseases and tuberculosis

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List of Abbreviations

AAFB	Acid alcohol-fast bacilli
AIDS	Acquired immunodeficiency syndrome
ARTI	Annual Risk of Tuberculosis Infection
BCG	Bacilli Calmètte Guérin
CDC	Center diseases and control
CLT	Central Laboratories for Tuberculosis
CXR	Chest X-ray
DOT	Directly Observed Treatment
DOTS	Directly Observed Treatment, Short course chemotherapy
DR	drug resistance
DST	Drug Susceptibility test
EMB	Ethambutol
EPI	Expanded Programme on Immunization
EPTB	Extra-Pulmonary Tuberculosis
F.B.S	Fasting Blood Sugar
FDC	Fixed-dose combination
GIT	Gastrointestinal tract
HIV	Human immune-deficiency virus
Hb	hemoglobin
ILT	Intermediate Laboratory for Tuberculosis
INH	Isoniazid
ITP	Individualized treatment regimen
IUATLD	International Union Against Tuberculosis and Lung Disease
MDR-TB	Multidrug-resistant TB
NTP	National Tuberculosis Control Programme
P.P.B.S	Post prandial blood sugar
PAS	Para amino salicylic acid
PIZ	Pyrazinamide
PTB	Pulmonary Tuberculosis
R.BCs	Red Blood Cells
RIF	Rifampicin

RMP	Rifampicin
SCC	Short course chemotherapy
SM	Streptomycin
STR	Standardized treatment regimen
TB	Tuberculosis
WBC	White Blood Cells
WHO	World Health Organization

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INTRODUCTION

Tuberculosis is a disease that is completely curable, yet kills more than two million people worldwide every year almost all of them in the developing world. In our fight against tuberculosis, we have a powerful weapon Tuberculosis is considered one of the most significant pathogens in terms of human morbidity and mortality ***(Lausardo and Ashken, 2000)***. It is estimated that by the year 2005, 12 million cases of tuberculosis will be occurring in the world annually, a 5.8% increase from 7.5 million estimated from 1990 ***(C.D.C. 1993).***

In 1993 WHO declared TB a global emergency, It is estimated by WHO worldwide that a nine million new cases of TB occurred and an estimated three million TB death.

According to the 9^{th} world health organization(WHO) annual report on surveillance planning for TB control , it calculated that there were 8.8 million new cases of TB in 2003 (140/100 000) , of which 3.9 million (62/100 000) were smear positive. There were 15.4 million prevalent cases (245/100 000), of which 6.9 million were smear positive (109/ 100 000). An estimated 1.7 million people (28/100 000) died from TB in 2003 including those co infected with HIV ***(WHO, 2005).***

Drug-resistant tuberculosis: This is a case of tuberculosis excreting bacilli resistant to one or more of anti-tuberculosis drugs. Basically, drug-resistance can be categorized into initial (primary) and acquired (secondary) ***(Crofton et al., 1997).***

Drug-resistant tuberculosis however is not a new phenomenon. Streptomycin-resistant M.Tuberculosis was described almost immediately after the introduction of streptomycin in 1944. Many patients who initially had improved, later relapsed despite continued therapy, on investigation, the failure was found to be due to the development of streptomycin resistant strains ***(Yaumans et al., 1946).***

The recent increase in drug resistance tuberculosis re-emphasizes the fundamental formula for tuberculosis control; early cause identification, combat and effective treatment completion of therapy until cure. Undelayed appropriate treatment aborts development of drug–resistant bacillary strains and blocks further disease transmission ***(Beck-Sange et al., 1992).***

The emergence of drug resistant strain of mycobacterium tuberculosis, especially Multidrug-resistant (MDR), defined as resistant to at least (INH) Isoniazid and

Rifampicin (RIF), Poses a thread to the success of tuberculosis (TB) control programmes ***(Pablos-Medez et al., 1997).***

MDR TB is an unwelcome reminder to wealthy countries that TB needs to be tackled as a worldwide issue. Globalization, migration via improved international transportation and the HIV pandemic further underscore the fact that wealthy countries cannot isolate themselves from efforts to control TB and MDR TB in the rest of the world.

However, more economically prosperous countries might wish to do so, especially if they have inherited a significant number of patients with Multidrug-resistant (MDR) tuberculosis from a period when treatment was unrecognized. The WHO tuberculosis control workshop held in Geneva (October 1995) recommended that a country prepared to go this expense should only provide these second-lines drugs for a specialized units in close connection with a laboratory able to carry out cultures and reliable susceptibility tests of M.Tuberculosis to the drugs ***(Crofton et al., 1997).***

The global magnitude of the problem is not well known. Most of the available studies are non-representative surveys of population or a country, frequently to discriminate between primary and secondary resistance. However emerging data suggest that, while Multidrug-resistance may not be a wide-

spread problem, it remains a public health threat in areas with a high prevalence of tuberculosis and sub-optimal tuberculosis control programs ***(Britton and Hopkin, 1998).***

Is MDR-TB really a problem?

Improper treatment and/or non adherence to treatment are most responsible for the new emergence of drug resistant strains. Accordingly, tuberculosis should be treated with at least two medications to which the organism is susceptible. A corollary of particular current importance is that directly observed to swallow the drug or receive the injection, is the only absolute certification of uninterrupted therapy ***(Weiw et al., 1994).***

AIM OF THE WORK

The present work was aiming to study the problem of drug resistance among newly diagnosed and retreatment cases of persistent smear positive pulmonary TB who were admitted to Abbassia Chest Hospital and registered in the chest clinics in Cairo 2004.

Spot light on tuberculosis history

Tuberculosis is a disease of great antiquity what were almost certainly tuberculous lesions have been found in the vertebrae of Neolithic man in Europe and of Egyptian mummies. Perhaps as early as 3700 BC ***(Morse et al., 1964)***

Tuberculosis is older than recorded history. Spinal lesion characteristic of tuberculosis have been found in Neolithic human remains, and Egyptian tombs paintings demonstrate the classic gibbous formation of Pott's disease. The earliest writings suggestive of tuberculosis are from India approximately 700 B-C, describing a chronic pulmonary disease with wasting. In about 380 B-C, Hippocrates provided a detailed description of a pulmonary disorder called phthisis, literally "to melt" or "to waste away" ***(Savacool, 1986).***

In 1678, the Dutch anatomist Francisus Sylvius described a small hard nodule in the lungs of patients with known phthisis which he called tubercles. In 1839 Johann Schönlein first suggested the name tuberculosis, and 1861 Oliver Wendell Holmes used the term "The white plague" to bring attention to the devastating

prevalence of tuberculosis in society. The birth of the science of bacteriology in 1865 prepared the way for Robert Koch's historic report in 1882 describing Mycobacterium tuberculosis ***(Rossman and MacGregor, 1995).***

The disease of tuberculosis is a quintessential opportunistic infection and it has historically found that it's opportunistic among the poor, the sick and malnourished and in people of all social classes who are in close contact with a person with active tuberculosis ***(Murray and Mills, 1990).***

In 1885, Edward Livingston Trudeau established the first sanatorium for tuberculosis in the United States, the Saranac Lake Cottage sanatorium. He built a laboratory there to apply the bacteriological tools developed by Koch and was quick to recognize the diagnostic value of Wilhelm Roentgen's x-ray first reported in 1896 and hence, sanatoria became the focal point of tuberculosis treatment and clinical research ***(Keers, 1978).***

The Greek Physician Galen, practicing and writing outlined treatment principles that were not modified over the next millennium: rest, restraint of cough, chest plasters, astringents for