

INTRODUCTION

According to the World Health Organization, more than 2 billion people (one third of the world's population) are currently infected with the TB bacillus, it continues to be a leading cause of burden and death among infectious diseases worldwide (**WHO, 2009**).

Several non-communicable diseases (NCDs), such as DM, alcohol use disorders and smoking-related conditions, are responsible for a significant proportion of TB cases (**Lönnroth et al., 2010**).

The rise of NCDs is important for TB control for a variety of reasons. First, many NCDs are risk factors for TB, especially for progression from infection to disease due to negative impact on host defense mechanisms against *Mycobacterium tuberculosis* (**Cegielski and McMurray, 2004**).

Secondly, NCDs may complicate treatment and management of TB, due to clinical challenges (e.g. among people with DM) as well as behavioral challenges (e.g. among people with alcohol use disorders) (**WHO, 2009**).

Thirdly, TB can trigger or aggravate NCDs. For instance, TB, like other infections, can worsen glucose control

and trigger DM , and a history of TB, although not a classical risk factor for COPD, is one of the leading causes of lung sequelae and bronchiectasis, and has been identified as an independent risk factor for COPD in a recent review (**Salvi and Barnes, 2009**).

The link between TB and NCDs also creates opportunities for improved diagnosis and management of both. Presence of a NCD may indicate the need to actively screen for TB, especially in high-burden countries, which can help improve early and increase TB case detection (**Lönnroth and Raviglione, 2008**).

Smoking also affects the chance of cure from TB. Severity of TB at the time of diagnosis and risk of relapse has been linked to smoking. In addition, a few studies have found that smokers have a higher risk of death from TB and other poor treatment outcomes than nonsmokers (**Lin et al., 2007**).

Nicotine is hypothesized to act directly on nicotinic acetylcholine receptors on macrophages to decrease intracellular tumor necrosis factor- α production and, thus, impair intracellular killing of *M. tuberculosis* (**Wang et al., 2003**).

There is some evidence that DM leads to delayed culture conversion (**Guler et al., 2007**), and that the risk of death during

TB treatment is increased (**Dooley et al., 2009**) as was the risk of relapse (**Maalej et al., 2009**).

The association between silicosis and pulmonary TB has been well documented. Silicosis is caused by the inhalation of crystalline silica particles, almost always due to occupational environments, including mining, sandblasting, quarrying, ceramic working and iron smelting (**Rees and Murray, 2007**). but silicosis and silica dust exposure are not deemed risk factors for relapse or reinfection (**Murray et al., 2000**).

A narrative review of studies demonstrated the negative impact of various macro- and micro nutritional deficiencies on TB immunity. Although the exact biological pathways are not fully understood, it is clear that poor nutrition, and specifically protein deficiency, impedes the ability of the cell-mediated immune system to fight *M. tuberculosis*, as it does for other infections (**Cegielski and McMurray, 2004**).

Low BMI at the time of diagnosis has also been linked to risk of treatment failure, death during TB treatment and relapse (**Khan et al., 2006**).

Other chronic conditions, such as autoimmune and systematic disorders, chronic renal failure, liver failure, certain malignancies and a wide range of immunosuppressant treatments, are also associated with TB (**Jeon and Murray, 2008**).

AIM OF THE WORK

To study the impact of comorbid diseases on the clinical presentation and outcome of pulmonary tuberculosis patients admitted to Abbassia Chest Hospital in the period between February 2014 and September 2014.

TUBERCULOSIS THROUGH HISTORY

TB is an ancient disease. Signs of skeletal TB (Pott disease) have been found in remains from Europe from Neolithic times (8000 BCE), ancient Egypt (1000 BCE), and the pre-Columbian New World (**Asensio et al., 2008**).

Skeletal remains show prehistoric humans (4000 BC) had TB, and researchers have found tubercular decay in the spines of Egyptian mummies dating from 3000-2400 BC.

Tuberculosis caused the most widespread public concern in the 19th and early 20th centuries as an endemic disease of the urban poor. By 1918, one in six deaths in France was still caused by TB. After determining the disease was contagious in the 1880s, TB was put on a notifiable disease list in Britain, campaigns were started to stop people from spitting in public places, and the infected poor were "encouraged" to enter sanatoria that resembled prisons. Even under the best conditions, 50% of those who entered died within five years (**McCarthy , 2001**).

In 1946, the development of the antibiotic streptomycin made effective treatment and cure of TB a reality. Prior to the introduction of this drug, the only treatment (except sanatoria) was surgical intervention, including the "pneumothorax

technique", which involved collapsing an infected lung to "rest" it and allow tuberculous lesions to heal (**Shields T, 2009**).



Epidemiology:

The five countries with the largest number of incident cases in 2011 were India (2-2.5 millions), China (0.9-1.1 millions), South Africa (0.4-0.6 million), Indonesia (0.4-0.5 million) and Pakistan (0.3-0.5 million). India and China alone accounted for 26% and 12% of global cases, respectively. (**World Health Organization, 2012**).

Tuberculosis in Egypt:

The incidence of TB varies with age. In Egypt, it primarily affects adolescents and young adults.

Tuberculosis is still a major public health problem. Many indices can be used to estimate the disease in the community and to compare the same area in different periods. Such information will be of national significance(**Khattab et al., 1998**).

Madkour et al. (1981) studied that the changing picture of TB in Shoubra dispensary over the years 1973-1977 and reported that the total number of cases diagnosed as tuberculosis were 4.4% in relation to total number examined with no statistically difference in the incidence between 1973-1977. The total number of positive sputum specimens examined by direct smear was 8.6% in relation to the total number examined. The total numbers of positive culture were 11.05% in relation to the total number examined by culture. New cases detected with X-ray shadow consistent with tuberculosis and gave positive sputum were only 824 out of 2952 cases (27.9%).

Al-Maraghy A et al. (1993) showed that during the period of 1981-1985 out of 1471 suspected pulmonary tuberculous cases there were 395 cases (26.85%) confirmed pulmonary tuberculosis by positive direct smear.

From the beginning, the national tuberculosis control programme (NTP) recognized that the involvement of different health care institutions would be essential to the

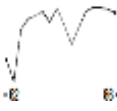
success of tuberculosis control in Egypt. Collaboration with partners outside the Ministry of Health and Population began as a mean to promote the Directly Observed Treatment Strategy (DOTS) within the Ministry, in the NTP's scientific and technical committees was the beginning to collaboration. As the NTP progressed, these committees provided the institutional structure to develop other partnerships with the private sector, nongovernmental organizations and prisons, involving them in tuberculosis control and spreading the message of DOTS.

Collaboration with the Health Insurance Organization (HIO), the main parastatal financier and provider of health services, has contributed significantly to case notification. Out of the 19, 000 new cases of tuberculosis that are expected to develop in Egypt annually, an average of 12, 500 new cases are detected each year. Of these, around 5500 are smear-positive pulmonary cases, 3000 are smear-negative pulmonary cases and 3000 are extra-pulmonary cases. In addition, 1000 relapse cases are notified annually. It is estimated that the NTP detects approximately 53% of the new smear-positive pulmonary tuberculosis cases (case detection rate, CDR), compared to the global WHO target of 70%. Rate of case detection of new

smear-positive cases rose slowly from 1991 to 1993 to just above 20%. Between 1993 and 1996 the rise accelerated, reflecting the improved coverage of case notification systems associated with DOTS expansion.

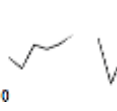
Like many other middle-income countries, Egypt has a significant private health care sector with over 50% of all utilization and expenditure on health care occurring in the private sector that is responsible for low case detection; In addition, the public sector is complex and there are a significant number of non government public and parastatal institutions responsible for providing and financing tuberculosis services. Finally, some people may not be accessing any health services, as financial, cultural and geographical barriers to seeking care **(WHO, 2004).**

New smear positive cases as a treatment outcome in Egypt

	Treatment success (%) 1995-2010	Year	Number notified	Size of cohort	Cohort as % notified	% of cohort					
						Cured	Completed	Died	Failed	Defaulted	Not evaluated
Egypt		1995	4, 229	2, 118	50	38	24	2	3	19	14
		2000	4, 606	4, 611	100	75	12	3	2	5	3
		2005	5, 217	5, 154	99	66	13	3	2	3	13
		2008	5, 102	5, 101	100	69	20	3	3	3	3
		2009	5, 201	5, 201	100	72	16	3	2	4	3
		2010	4, 679	4, 682	100	59	27	3	3	4	4

(WHO, 2011)

Retreatment cases as a treatment outcome in Egypt

	Treatment success (%) 1995-2010	Year	Number notified	Size of cohort	Cohort as % notified	% of cohort					
						Cured	Completed	Died	Failed	Defaulted	Not evaluated
Egypt		1995	753								
		2000	620	956	154	52	11	7	12	13	5
		2005	738	738	100	41	17	10	12	8	12
		2008	792	779	98	39	32	8	8	9	4
		2009	748	748	100	39	39	6	5	7	4
		2010	703	703	100	38	38	6	8	8	6

(WHO, 2011)

Sex-related demographics:

TB rates in women have declined with age, but in men rates have increased with age. In addition, men are more likely than women to have a positive tuberculin skin test result. The estimated sex prevalence for TB varies by source, from no sex prevalence to a male-to-female ratio in the United States of 2:1 (Menzies et al., 2007).

Age-related demographics:

Higher rates of TB infection are seen in young, nonwhite adults (peak incidence, 25-40 years) than in white adults. In addition, white adults manifest the disease later (peak incidence, age 70 years) than do nonwhite persons.

In the United States, more than 60% of TB cases occur in persons aged 25-64 years; however, the age-specific risk is highest in persons older than 65 years. TB is uncommon in children aged 5-15 years (WHO, 2010).

Pathology of tuberculosis:

The main cause of TB is *Mycobacterium tuberculosis*, a small, aerobic, nonmotile bacillus with an outer membrane lipid bilayer; it was discovered by Robert Koch and had been published in 1882 as a slow growing *Mycobacterium tuberculosis* (**Madigan et al., 2012**).



Dr. Robert Koch

The high lipid content of this pathogen accounts for many of its unique clinical characteristics. It divides every 16 to 20 hours, which is an extremely slow rate compared with other bacteria (**Niederweis et al., 2010**).

If a Gram stain is performed, *Mycobacterium Tuberculosis* (MTB) either stains very weakly "Gram-positive" or does not retain dye as a result of the high lipid and mycolic acid content of its cell wall. MTB can withstand weak disinfectants and survive in a dry state for weeks. In nature, the bacterium can grow only within the cells of a host organism, but MTB can be cultured in the laboratory **(Madison, 2001)**.

Using histological stains on expectorated samples from phlegm (also called "sputum"), scientists can identify MTB under a regular (light) microscope. Since MTB retains certain stains even after being treated with acidic solution, it is classified as an Acid-Fast Bacillus (AFB) **(Madison, 2001)**.

The most common acid-fast staining techniques are the Ziehl-Neelsen stain, which dyes AFBs a bright red that stands out clearly against a blue background, and the auramine-rhodamine stain followed by fluorescence microscopy **(Piot et al., 2008)**.

Risk factors:

A number of factors make people more susceptible to TB infections. The most important risk factor globally is HIV; 13% of all TB cases are infected by the virus. This is a particular problem in sub-Saharan Africa, where rates of HIV are high. Tuberculosis is closely linked to both overcrowding and malnutrition, making it one of the principal diseases of poverty **(Chaisson et al., 2008)**.

Factors in acquiring TB infection:

The number of bacilli in the inoculum and the relative virulence of the organism are the major factors determining transmission of the diseases, whereas cavitory lesions have 10 million to one billion bacilli. Thus, persons with cavitory lesions are highly infectious. Also, contacts of persons with sputum-positive smears have an increased prevalence of infection as opposed to contacts of those with sputum-negative smears. Persons who have received anti-TB drugs are much less infectious than those who have not received any treatment. (Leung, 2010).

Environmental factors also like ventilation of the surroundings and exposure to ultraviolet light. Thus, overcrowding, congregation in prison settings, poor housing, and inadequate ventilation predispose individuals to the development of TB (Blumberg et al., 2003).

Factors in acquiring TB disease:

Defects in cell-mediated immunity (CMI) and level of immune competence are major determinants for development of disease. In fact, infection with HIV is one of the most significant risk factors for TB infection. Steroid therapy, cancer chemotherapy, and hematologic malignancies increase the risk of TB. In addition, malnutrition interferes with the CMI response

and therefore accounts for much of the increased frequency of TB in impoverished patients. Non-TB infections, such as measles, varicella, and pertussis, may activate quiescent TB **(Taylor Z et al., 2005)**.

Individuals with certain human leukocyte antigen (HLA) types have a predisposition to TB. Hereditary factors, including the presence of a Bcg gene, have been implicated in susceptibility to acquisition of this disease **(Critselis et al., 2012)**.

Although anyone can become infected with TB, some people are at a higher risk, such as:

- Poor or homeless people.
- Foreign-born people who come from countries with endemic TB.
- Older people, nursing home residents, and prison inmates.
- Alcoholics and intravenous drug users.
- Those who suffer from malnutrition.
- Diabetics, cancer patients, and those with HIV/AIDS or other immune system problems.
- Healthcare workers.
- Workers in refugee camps or shelters.

(Mayo Clinic, 2012)