The Impact of Comorbidities on the Outcome of Tuberculous Patient in Respiratory Intensive Care Unit

Thesis

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ABSTRACT

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

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

Aim of the work: there are limited data regarding active pulmonary tuberculosis (APTB) patients requiring ICU admission. This study aimed to determine the mortality rate and risk factors associated with TB patients with comorbidities requiring respiratory intensive care unit (RICU) admission**.**

Patients and methods: a combined retrospective-prospective study was conducted from November 2014 to October 2016 and from November 2016 to April 2017 on adult patients with APTB admit to the RICU of Abbassia Chest Hospital for a period of more than 24 h. Demographic, clinical and therapeutics characteristics as well as outcome (RICU morality) were obtained from the medical records.

Results: in this study a total of 43 patients were considered (median age 45 years for non survived patients and 36 years for survived patients). The RICU morality rate was 81.4%. Respiratory failure was the most common cause of admission to RICU 37,2% (16 patient). Mechanical ventilation (MV) was needed in 69.8% of patients (30 patients). Death rate in the diabetic patients was14.29%, in patients with renal disease it was 20% , in case of HIVit was 17.14% and in case of malignancy it was 8.57%.There was highly significant mortality rate accompanying LCF and the ratio was 31.43%,in case of respiratory failure type II it was 94.28% and in mechanical ventilation it was 80%. Non survived patients had high significant APACHE SCORE 21.4±6.2 and the main cause of death was mainly ventilatory 80%(28 patients).

Conclusion: the present study showed a very high mortality rate among TB patients with comorbidities requiring respiratory intensive care unit (RICU) admission and identified associated co morbidities, risk factors and a predictor of RICU mortality.

Keywords: active pulmonary tuberculosis, mortality, respiratory intensive care unit, co morbidities.

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List of Abbreviations

ATT	: Antituberculosis therapy
CDC	: Centers for Disease Control and Prevention
COPD	: Chronic Obstructive Pulmonary Disease
CTLs	: Cytotoxic T lymphocytes
DM	: Diabetes mellitus
DTH	: Delayed-type hypersensitivity
HIV	: Human immunodeficiency virus
ICU	: Intensive Care Unit
IFN	: Interferon
IL	: Interleukin
LAM	: Lipoarabinomannan
LTBI	: Latent tuberculosis infection
MHD	: Maintenance Haemodialysis
NCDs	: Non-communicable diseases
PDIM	: Phthiocerol dimycocerosates
PGL	: Phenolic glycolipid
RNI	: Reactive nitrogen intermediates
SSA	: Sub-Saharan Africa
TB	: Tuberculosis
TDM	: Trehalose dimycolate

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Introduction

According to the World Health Organization, more than 2 billion people (one third of the world's population) are currently infected with the tuberculosis (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).***

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 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, 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 immune-suppressant treatments, are also associated with TB ***(Jeon and Murray, 2008).***

Aim of the Work

To study the impact of comorbid diseases on the outcome of pulmonary tuberculosis patients admitted to ICU at Abbassia Chest Hospital in the period between november 2014 to October 2016 (retrospective part) and between November 2016 to April 2017 (prospective part) .

Tuberculosis

Tuberculosis is an infectious disease caused by the bacillus Mycobacterium tuberculosis. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB). The disease is spread in the air when people who are sick with pulmonary TB expel bacteria, for example by coughing. In general, a relatively small proportion of people infected with M. tuberculosis will develop TB disease; however, the probability of developing TB is much higher among people infected with HIV. TB is also more common among men than women, and affects mostly adults in the economically productive age groups ***(Global Tuberculosis Report, 2013).***

Historical aspects of tuberculosis:

Tuberculosis (TB) has a long history. It was present before the beginning of recorded history and has left its mark on human creativity, music, art, and literature; and has influenced the advance of biomedical sciences and healthcare. Its causative agent, Mycobacterium tuberculosis, may have killed more persons than any other microbial pathogen ***(Daniel, 2006).***

TB was documented in Egypt, India, and China as early as 5000, 3300, and 2300 years ago, respectively ***(Daniel, 2006)***.

Typical skeletal abnormalities, including Pott's deformities, were found in Egyptian and Andean mummies and were also depicted in early Egyptian and pre-colombian art ***(Sotomayor et al., 2004).***

One of the greatest works on TB was performed in 1882 by Robert Koch, an esteemed scientist of his time. Koch isolated and cultured M. tuberculosis from crushed tubercles. His experimental work identified the bacterium as the TB etiological agent ***(Daniel, 2006)***.

The tuberculin skin test became the principal tool for infection diagnosis. In the same period, Koch developed staining methods for the identification of the bacillus; these techniques were subsequently improved by the German Doctor and bacteriologist Paul Ehrlich, whose method for detection of the bacillus provided the basis for the development of the Ziehl-Nielsen staining, which still is an important tool to diagnose TB ***(Ducati et al., 2006)***.

In 1900, Calmette and Guerin discover the vaccine (BCG) that was obtained from attenuation of a strain of Mycobacterium bovis ***(WHO, 2012).***

Streptomycin (1943), P- amino salicylic acid (1949), Izonaizid (1952), Pyrazinamide (1954), cycloserine (1955), Ethambutol (1962) and Rifampicin (1963) were introduced