ADENOSIN DEAMINAS ACTIVITY IN SERUM AND PLEURAL FLUID IN TUBERCULOUS AND NON – TUBERCULOUS PATIENTS

Thesis

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BY

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Introduction

Tuberculosis (TB) is considered today as the most important re-emerging disease worldwide. The prevalence varies enormously between countries. The global TB epidemics has increased largely due to an increase of 25% infection rate in African countries because of co-infection with HIV ***(Aldrich, 2000) (Barankiewicz and Cohen, 1984) (Iseman, 2000)***

Adenosine deaminase plays a role in the proliferation and differentiation of lymphocytes. It is present more in T-Lymphocytes than B-Lymphocytes and increases during T-cell differentiation. ***(Raviglione, 1998)***

Adenosine Deaminase (ADA) is an enzyme which is involved in purine catabolism and in responsible for the conversion of adenosine deoxyadenosine to inosine, deoxyinosine respectively and amonia. Further metabolisation of these deaminated nucleosides leads to hypoxanthine. ***(Raviglione, 1998) (Who press, 2001)***

The high sensitivity and specificity of ADA for an early diagnosis of tuberculous plural effusion is promising.

Aim of the work

To evaluate the usefulness of ADA (Adenosine Deaminas) as a biomarker in diagnosis of TB pleural effusion by comparing both serum and pleural effusion levels.

Tuberculosis burden

Historical background

Tuberculosis (TB) has been important disease throughout human history. The earliest archaeological evidence of human TB comes from Egyptian art and mummies, there is sample evidence of spinal TB (Pott's disease) as early as 5,500 years ago**.** Almost 2,500 years ago, the famous Greek doctor Hippocrates said that tuberculosis was the most common disease of his time **(Daniel, 1997)**

Tuberculosis was called consumption because it consumed the person from within. It was also known as the white plague because victims were so pale from loss of blood. TB also has been called scrofula, the Latin word for female pig, sometimes TB bacteria infect glands in the neck, which swell up like a pig's neck. For a long time, TB was called Koch's disease after Robert Koch, the man who discovered Mycobacterium tuberculosis (MTB**) (Murray and Mills, 1990).**

In the Nineteenth century, some doctors suggested building special TB hospitals in places believed to be healthy for people with tuberculosis. Sanatorium is from the Latin word meaning "to cure." Each sanatorium was a special clinic where people with TB would go to get better. They removed infectious patients from the rest of the population. In 1865, a French army doctor named ***Jean Antoine Villemin*** took fluids from humans who had TB and injected them into rabbits. The rabbits got tuberculosis as well. This proved that the disease was contagious, but it still did not explain how the infection took hold. A few years later, in 1882, a German doctor named ***Robert Koch*** made medical history when he had found the germ that causes tuberculosis **(Barnes and David , 1996).**

In the Twentieth century, after Koch proved there was a tuberculosis germ, doctors and researchers invented new tools to diagnose the disease. In 1908, researchers developed the skin test for TB still used today. Anti-tuberculosis drug treatment started in 1944, when streptomycin and para amino salicylic acid (PAS) were discovered. In 1952, a third drug, isoniazed, was added to

the previous combination, greatly improving the efficacy of treatment, but which still had to be administered for 18-24 months. In 1960, ethambutol (EMB) substituted PAS, and the treatment course was reduced to 18 months. In the ’70s, with the introduction of Rifampicin(RMF) into the combination, treatment was shortened to just nine months. Finally, in 1980, Pyrazinamide (PZA) was introduced into the anti-tuberculosis treatment, which could be reduced further to only six months **(Yancey, 2007).**

In 1990, the World Health Organization (WHO) developed the directly observed therapy strategy (DOTS) to limit the burden of TB. And effective diagnosis and treatment of TB has saved about 43 million lives between 2000 and 2014. Mortality rate of TB has fallen 47% since 1990 and its incidence has fallen by an average of 1.5% per year since 2000 and is now18% lower than the level of 2000 (**WHO, 2015).**

The history of TB reveals that this disease has swept across large regions of the globe in slowly moving epidemic waves with periods measured in centuries. The factors contributing to the rise and decline of these waves are only partly known and are difficult to control in the absence of massive social and political changes **(Kochi, 1991).**

Epidemiology of tuberculosis

- ***Global epidemiology:*** **(WHO , 2016)**

Tuberculosis is still a major cause of death worldwide and there are still major threats to global TB control as Poor social conditions due to inadequate housing and nutrition, immune compromise related to humman immune-deficiency virus (HIV) pandemic and emergence of drug-resistant TB. It is one of the top 10 causes of death worldwide. Globally in 2015, the number of TB deaths was 1.4 million (among HIV negative people) and 0.4 million (among HIV positive people). The number of TB deaths fell from 1.8 million in 2000 to 1.4 million in 2015. However, the global rate of decline in the TB incidence rate was only 1.5% from 2014 to 2015 and the case fatality ratio in 2015 was 17%. Worldwide in 2015, there were an estimated 10.4 million incident TB cases. An estimated 62% of these cases were male, and 90% of cases were adults. Six countries accounted for 60% of the global total: India, Indonesia, China, Nigeria, Pakistan and South Africa. Globally in 2015, there were an estimated 480 000 new cases of multiple drugs resistant TB (MDR-TB) and an additional 100 000 people with rifampicin-resistant TB

(RR-TB) who were also newly eligible for MDR-TB treatment; India, China and the Russian Federation accounted for 45% of these cases. Following WHO guidance issued in May 2016, all cases of RR-TB, including those with MDR-TB, should be treated with a second-line MDR-TB treatment regimen. Globally, about 3.3% of new TB cases and 20% of previously treated cases have MDR-TB and about 9.7% of people with MDR-TB have extensive drug resistant TB (XDR-TB). **(Figure 1&2)**

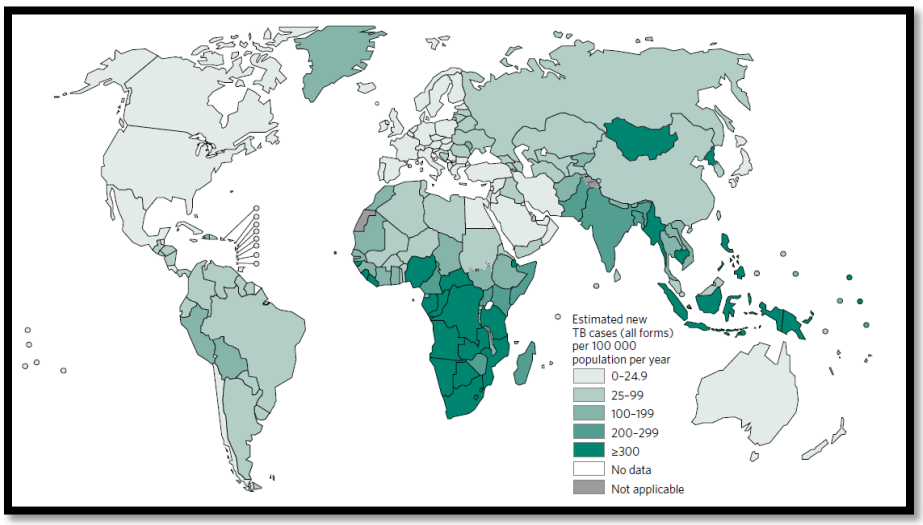

Figure (1): Estimated TB incidence rates (WHO, 2015)

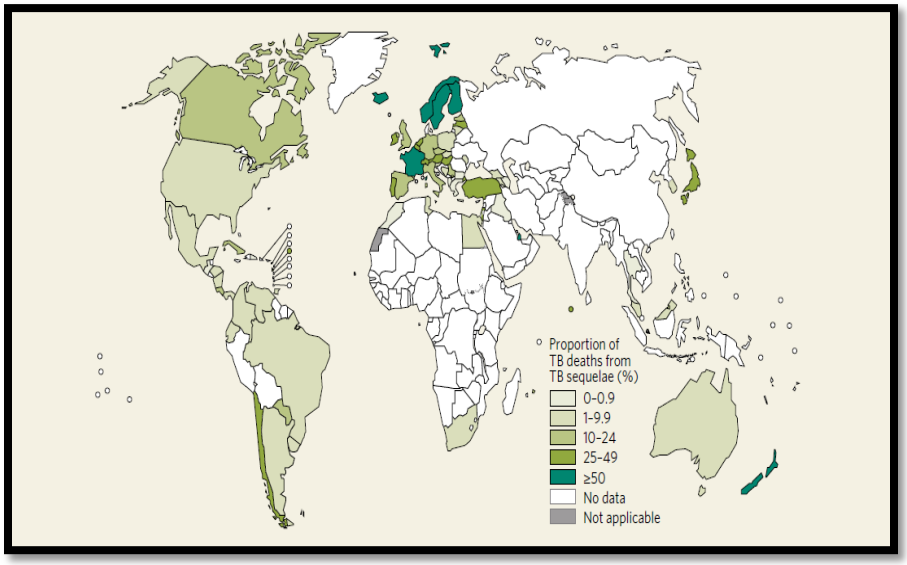

Figure (2): Deaths from TB sequelae as a portion of the total number of TB deaths (WHO, 2015)

Epidemiology of tuberculosis in Egypt

Egypt is ranked as a country with middle / low level of tuberculosis incidence .It is estimated that TB incidence rate was about 15 cases per 100 000 population in 2015.**(WHO, 2015)** ***(table 1 and figure 3&4)***

Table(1):Estimated burden of TB cases in Egypt 2015 (WHO,2015)

Population 2015		**92 million**
Estimates of TB burden*, 2015	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	0.22 (0.2–0.24)	0.24 (0.21–0.26)
Mortality (HIV+TB only)	0.018 (0.012–0.025)	0.02 (0.01–0.03)
Incidence (includes HIV+TB)	13 (12–15)	15 (13–16)
Incidence (HIV+TB only)	0.053 (0.042–0.065)	0.06 (0.05–0.07)
Incidence (MDR/RR-TB)**	2.2 (1.8–2.6)	2.4 (2–2.8)