Epidemiological Study of Tuberculosis Pattern and Management in a Sample of Egyptian Children (Abbassya Chest Hospital)

Thesis

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List of Abbreviations

AFB	**Acid fast bacilli**
AIDS	**Acquired immuno-deficiency syndrome**
ARI	**Annual risk of infection**
BCG	**Bacillus Calmette Guerin**
BC	**Before Christ**
CDC	**Center of disease control**
CSF	**Cerebro spinal fluid**
DM	**Diabetes mellitus**
DNA	**Deoxyribo nucleic acid**
DOTS	**Direct observed therapy of short duration**
EIA	**Enzyme immuno-assay**
ELISA	**Enzyme linked immunosorbent assay**
ESR	**Erythrocyte Sedimentation rate**
E	**Ethambutol**
HIV	**Human immunodeficiency virus**
HLA	**Histocompatibility leucocytic antigen**
H or INH	**Isoniazid**
IUATLD	**International Union Against Tuberculosis and Lung Diseases**
MDR	**Multiple drug resistance**
MGIT	**Mycobacteria growth indicator tube**
MRI	**Magnetic Resonnance Imaging**
MoH&P	**Ministry of Health and Population**
MOTT	**Mycobacteria other than tubercle bacilli**
MTB	**Mycobacterium tuberculosis**
NTCP	**National Tuberculosis Control Program**
NTM	**Non-tuberculous mycobacteria**
NTP	**National Tuberculosis Program**
OT	**Old tuberculin**
PAS	**Para-aminosalicylic acid**
PCR	**Polymerase chain reaction**
PPTB	**Positive pulmonary tuberculosis**
PPD	**Purified protein derivative**
RBC	**Red Blood Cell**
RIF or R	**Rifampicin**
SD	**Standard Deviation**
S	**Streptomycin**
T	**Thiacetazone**
TB	**Tuberculosis**
TU	**Tuberculin unit**

UK	**United Kingdom**
U/S	**Ultra-sound**
US	**United States of America**
WBC	**White Blood Cell**
WHO	**World Health Organization**
Z	**Pyrazinamide**
ZN	**Ziehl – Neelsen**

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Introduction and Aim of the Work

Tuberculosis is a major, cause of morbidity disability and mortality throughout the world. Tuberculosis killed 2.5 million people in the world in 1990 and 98% of them were in the developing countries (Raviglione et al., 1995). Pulmonary Tuberculosis (PTB) remains one of the most important health problems in the world with an estimated 8 millions new cases of pulmonary tuberculosis and 1.9 million deaths having occurred in1997 (Conde et al.2000).

Frequent data from WHO show a world-wide increase in the number of yearly reported cases (WHO, 1994).WHO estimates more than 8 million new cases of tuberculosis occur and approximately 3 million people die of the disease worldwide each year. Almost 1.3 million cases and 450,000 deaths occur in children each year. If the present trend continue, 10.5 million new cases are expected to occur annually by 2005 with Africa having more cases than any other region in the world. (Munoz and Starke, 2004). The recurring spread of tuberculosis epidemic in recent years was associated with the spread of AIDS which weakens the body's immunity (Tag El-Din, 2002).

As a member of the Eastern Mediterranean Region of the WHO, Egypt is considered as a member country with moderate prevalence of tuberculosis with estimated incidence 25-29 per 100,000 population (WHO, 2001) and the report from Egyptian National TB Program revealed that the annual risk of TB infection is 0.32% and that the incidence of smear positive cases is 16 per 100,000 population (ElMoghazy, 1997). The total number of TB cases reported in 1999 was 11763 and the number of new smear positive cases was 5095 (WHO, 2001). The case fatality rate for TB was 50% for untreated patients before the advance of antibiotic therapy. Deaths worldwide are estimated at 3 million per year. Mortality of untreated congenital TB is 50% (Lobata et al., 2000&ATS/CDC, 2003).

The social stigma attached to tuberculosis may be linked to the long term debilitation and discomfort it produces in contrast to other short term infectious diseases and yet the threat it poses to the economic stability and health of the entire family particularly when the bread winner is affected (Brieger and Carl, 1992).

Studies show that traditional factors associated with tuberculosis such as poverty, homeless, malnutrition, overcrowding, drug and alcohol abuse are also contributing to the increase of tuberculosis (Zolopa et al., 1994). Infection in children is typically due to prolonged close contact with an individual having untreated, active, cavitary, sputum-positive disease (Prince, 1998).

Children can be a real threat since primary infection can progress quickly to active disease and serious complications as miliary tuberculosis and meningitis may occur (Tuberculosis Control Guide, 1999). The American Academy of Pediatrics reported an increase in tuberculosis infection by 34% among children aged 5-14 years and 36% among those younger than 5 years old (Butlaro and Ezell, 1995). Fifty percent of 0-14 years old, house-hold contacts of smear positive cases became tuberculin positive, but only 5% converted when contact case was culture positive but smear negative (Styblo, 1980).

Patients at risk of infection with resistant strains were those who failed to complete a prescribed course of therapy or were otherwise non-compliant (Bass et al., 1990).

There are five clinical thought to be the most relevant as predictors of the disease in children: history of contact with a case of tuberculosis, positive skin test, persistent cough, low weight for age and unexplained or prolonged fever (Fourie et al., 1998).

The only available vaccine against tuberculosis is Bacille Calmette – Guerin (BCG), named for the two French investigators responsible for its development. The route of administration and dosing schedule for BCG vaccine are important variables for its efficacy. The preferred route of administration is intradermal injection with a syringe and needle because it is the only method that permits accurate measurement of an individual dose (Fisherman, 2002&Munoz and Starke, 2004).

Aim of the Study

1-To assess a general knowledge and to study the epidemiology of tuberculosis among a sample of Egyptian children admitted in Abbassya Chest Hospital throughout 5 years.

2- To study the distribution of tuberculosis as regard various aspects: age, sex, resident, BCG vaccine scar, presenting symptoms, contact history, tuberculin test, laboratory and bacteriological finding.

3-To study the clinical picture of tuberculosis in children, to report any recent changes in its symptoms and signs and to detect any complications.

4-To study the laboratory and radiological findings of tuberculosis in Egyptian children and to report any significant changes.

History of Tuberculosis

Tuberculosis is an ancient disease

The earliest records that are consistent with tuberculosis are the Egyptian wall paintings that depict typical hunchback deformities and correlate with findings of spinal TB in mummies (Morse et al., 1964&Fisherman, 2002). In addition, the recent finding of acid and alcohol fast bacilli in human remains coming from human skeleton in Heidelberg, Germany, dating back to 5000 B.C (Sager et al., 1972), similar proof has been obtained from Egyptian mummies from around 3500 B.C (Zimmerman,1979). Other example of prehistoric tuberculosis includes a mummy from 1000 B.C revealed not only Pott`s disease of the spine but also a psoas abscess (Morse, 1961). Furthermore, there is evidence that a large sanatorium for treating victims of tuberculosis existed in Egypt about 1000 B.C (Dubos, 1982).

The first written description of TB is from India 700 B.C. In first writing it was called consumption because its tendency to produce great wasting in its victim. In the nineteenth century it was known as the white plague and eventually the name acquired with the discovery of the tubercle bacillus by Robert Koch in 1882(Baum and Wolinsky, 1983&Fisherman, 2002).

An affliction of man kind from the dawn of civilization, tuberculosis is accurately described (fever, cough coupled with expectoration of blood and sputum and generalized wasting suggestive of pulmonary tuberculosis), in the earliest writing of Chinese and Roman physicians (Keers, 1981). Greek literature contains numerous references to conditions resembling consumption (tuberculosis) including Hippocrates, who lived between 460-377 B.C., probably introduced the term phthisis, the old name of tuberculosis (Meachen, 1978), Aristotle (384-322 B.C.) who recognized the contagious nature of the disease and Plato (430-347 B.C) who recommended no treatment because caring for chronic tuberculotic patients was of no advantage to the patient (Evans, 1998).

In Northern Europe, Britain, France and Germany, the notion existed that tuberculosis was indeed hereditary, that one inherited the tuberculous diathesis bacilli. Robert koch in 1882, described tubercle bacilli using aniline dyes and oil immersion microscope and was able to identify tubercle bacilli in every lesion in the human or animal victim and was able to culture the bacillus outside the body. Furthermore, he inoculated the bacillus into an experimental animal that developed tuberculosis. Henceforth, searching for the bacillus in sputum of suspected cases quickly became standard clinical practice (Sakula, 1982).

Finally, in 1896 Roentgen (1845-1923) announced the discovery of x- ray and was quickly applied to the disorder of chest and tuberculosis in particular (Evans, 1998).

Etiology of Tuberculosis

The genus *Mycobacterium* "fungus like bacterium" was first described by Lehmann and Neurmann, and includes *Mycobacterium leprae* and *Mycobacterium tuberculosis* (Evans, 1998). It is one of the most widely distributed bacterial genera in nature. Since Koch's description of the human tubercle bacills in 1882, many other species of Mycobacterium have been isolated and characterized (Songer, 1981).

Currently, there are 71 recognized species in the genus *Mycobacterium*. These species produce a spectrum of infections in humans and animals (Forbes et al., 1998).

There are five closely related mycobactria in the Mycobactrtium tuberculosis complex: M. tuberculosi, M .bovis, M. africanum, M. microti, and M. canneti . All belong to the order of Actinomycetales and the family of Mycobacteriacae . M. tuberculosis is the most important cause of tuberculosis disease in humans (Munoz and Starke, 2004).

The tubercle bscilli are non- spore forming, non motile, pleomorphic, weakly gram-positive curved rods 2-4umlong. They may appear beaded or clumped in stained clinical specimens or culture media. They are obligate aerobes that grow in synthetic media containing glycerol as the carbon source (e.g. Loewenstein Jensen culture media). These mycobacteria grow best at 37-41°c, produce niacin, and lack pigmentation. A lipid- rich cell wall accounts for resistance to the bactericidal actions of antibody and complement. A hallmark of all mycobacteria is acidfastness .Once stained they resist decoloration with ethanol and hydrochloric or other acids (Starke, 2001).

Atypical mycobacteria: The term Non Tuberculous Mycobacteria (NTM) includes all other mycobacterial species that do not belong to the (typical) M.*tuberculosis* and *M. bovis* complex. This large group has been known by several names; Atypical, Enviromental, Opportunistic, Mycobacteria other than tubercle baclli (MOTT), unclassified, or Anonymous (Debrunner et al., 1992) . This group can cause disease which may be clinically, radiologically and histopathologically indistinguishable from tuberculosis . The disease associated with them has been termed pseudo-tuberculosis or Mycobacteriosis (Hanaks, 1968).

The main difference between (MOTT) and *M.Tuberculosis* is that MOTT is ubiquitous environmental organisms and not transmitted from person to person (Kuyp, 1997). NTM are present everywhere in the environment and sometimes colonize in healthy individuals in the skin, respiratory and gastrointestinal tract (Portaels, 1995).

In Egypt, Hussien et al. in 2000 stated that 87% of all isolated strains were *M. tuberculosis*, and 13% were atypical strains: 6.5% *M. avium*-intracellular, 4.5% *M. Kansas* and 2.2% *M. chelonei*. El Gazar et al. in 1998 found that 12.7% of isolates were atypical strains ; 8.5% *M. avium*-intracellulare; 4.2% *M. chelonei*. Gamal El Din in 1997, found atypical strains in 14% of the isolates. Lower results were obtained by Othman in 1993, in Sharkia governorate who found atypical strains in 7.7%.