

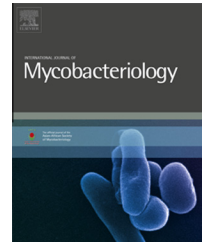
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Review

Mapping the epidemiology and trends of extra-pulmonary tuberculosis in Saudi Arabia



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ABSTRACT

An extra-pulmonary tuberculosis (EPTB) infection rate of 30% in Saudi Arabia remains above the global rate. A variable rate of infection in each province has been reported and the involvement of most organs has been cited. Nationwide collective data on the current trends of infection are scarce and the factors behind the increased rate of EPTB are perplexing. This review endeavors to shed light into the epidemiology of EPTB, various types of infections sites, geographical differences in the infection rate, known risk factors, and challenges in the diagnosis and management of EPTB in Saudi Arabia.

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Introduction

Despite the developments in treatment and diagnosis, tuberculosis (TB) remains an enormous public health problem [1]. A decreasing or stable trend of new TB cases was observed from developed or industrialized nations. However, some developing countries show an increasing trend, whereas many others exhibit a very slow decline in incidence [1]. TB is primarily a disease of the lungs (pulmonary tuberculosis [PTB]), but can affect almost any organ in the body and the occurrence at sites other than the lung is defined as extra-pulmonary tuberculosis (EPTB). Despite the fact that EPTB is a serious clinical problem because of the diagnostic challenges encountered and the propensity to cause high morbidity and mortality, it receives less interest mainly due to low infectious potential [2,3]. The deadly synergisms between TB and human immunodeficiency virus (HIV) with the emergence of drug resistance have complicated the control of TB globally.

Extra-pulmonary involvement of mycobacteria can mostly happen through the lymphatic or hematogenous dissemination to any part of the body. In addition, the bacteria can stay dormant for a very long time. Due to higher efficacy in infecting any organ, the mycobacterium has a wide variety of clinical manifestations. Additionally, EPTB poses certain challenges in its diagnosis and management, even in resource-rich countries. The diagnosis is always cumbersome owing to the wide spectrum of clinical presentations, limited specificity of manifestations, and difficulties in obtaining specimens for diagnosis [4]. When considering the diagnostic difficulties of EPTB, the real magnitude of the problem at the community level may be underestimated, even with the current management system in most countries, including Saudi Arabia. To draw attention towards the magnitude of EPTB infections, in this review we attempted to show the current understanding of the epidemiology of EPTB, diversity in its clinical presentations, and the future research prospects required in Saudi Arabia.

Global trend on epidemiology and clinical pattern of EPTB

EPTB has been reported in almost all global regions, particularly in developed countries [1,4,5]. The World Health Organization data shows 0.8 million EPTB cases among the 6.1 million of new TB cases reported in 2013 [1]. The HIV epidemic, rising numbers of immigrants from developing countries to developed countries, and a fair amount of immune disorders are assumed to be responsible for this rise in TB cases in many countries [1–3,6,7]. A 10-year surveillance data from the European Union (EU) showed an increasing trend of EPTB in the member states [8]. A 13 year data from

the United States also showed an increasing proportion of EPTB compared with the decreasing trend of PTB [9].

Trends of clinical patterns of EPTB in most global regions were highly diverse in presentation. In the USA, a nationwide report shows lymphatic TB (40.4%) as the most prominent followed by pleural TB (19.8%), bone and joints TB (11.3%), genitourinary (6.5%), tuberculous meningitis (5.4%), peritoneal (4.9%), and 11.8% of other sites [9]. However, in the EU, the trend was different as it showed a higher predominance of pleural TB (36.7%), followed by lymphatic TB (30.5%), genitourinary (6.9%), bone and joints (5.1%), central nervous system (4.4%), gastrointestinal (2.7%), and other sites (9.4%) [8]. Recent data from Brazil also showed a similar trend to the EU, with the dominance of pleural TB (42%) followed by lymphatic TB (21%), meninges (6%), bone (5%), genitourinary (3%), miliary (8%), and others (15%) [10]. Nationwide data or large scale data were scarce from the major TB endemic regions of Africa and Asia.

Epidemiology of EPTB in Saudi Arabia

Annual case rates of EPTB have been recorded in Saudi Arabia since 1989. A considerable drop in the rate of incidence was reported in the initial period. However a gradual increase was evident since 1994 [11]. In 1991, the proportion of EPTB in the country was 11.7% of the total reported TB cases, followed by a sharp increase to 28.2% in 1997 [12,13]. However, a recent national TB notification registry data showed a consistent level of EPTB cases in the country – around 30% of total reported TB cases annually [14,15]. Fig. 1 explains the incidence rate of EPTB reported during 2005–2012. Interestingly, recent trends show a slight decrease in the rate of EPTB in connection with the decreasing trend of total notified TB cases in the country. The incidence rate ranges from 3.5–5 cases/10⁵ population in recent years when compared with the total TB incidence of 17–21 cases/10⁵ population in the same period [14,15]. Nonetheless, a variation of EPTB proportions was reported from several institutions, ranging from 15% to 63%. However, these data are based on a single institution and thus a nationwide picture could not be possibly drawn. A recent nationwide study conducted only with culture positive cases reported 20% EPTB among the 1904 patients examined [16–20].

Until now there were only two nationwide studies that looked deep into the clinical features and epidemiology of EPTB in the country [21,22]. Memish et al. [21] reported on the incidence and risk factors of EPTB on nationwide data collected during 2010–2011 from the national disease notification system. The data covered all the provinces of the country through the current TB notification system. The data showed

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