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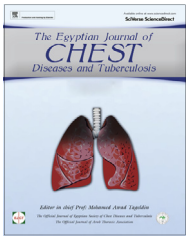

ORIGINAL ARTICLE

Detection of extensively drug resistant pulmonary tuberculosis

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Abstract *Introduction:* The rise in human immune virus infections (HIV) and the neglect of tuberculosis (TB) control programs have enabled a resurgence of TB. The emergence of drug-resistant strains has also contributed to this new epidemic from 2000 to 2004, with, 20% of TB cases being resistant to standard treatments and 2% resistant to second-line drugs. The rate at which new TB cases occur varies widely, even in neighboring countries, apparently because of differences in health care systems.

Aim of the work: The aim of the current study is to investigate susceptibility to anti-TB drugs in newly diagnosed and old TB patients (with persistent positive sputum smear after 2 months of anti-TB treatment) for detecting multi-drug resistance (MDR-TB) and extensively drug resistant TB (EDR-TB). As well, find out risk factors associated with the development of MDR and XDR-TB.

Patients and methods: The study included 40 strains of mycobacterium TB. These strains were divided into two groups: Group I: 20 strains isolated from new cases (patients who had never treated for TB or who have taken anti TB drugs for less than 1 month). Group II: 20 strains isolated from old cases (Patients with persistent positive sputum smear after 2 months of anti-TB treatment). After taking an informed consent, all subjects were subjected to: Detailed history taking, complete clinical examination, anthropometric measurements, routine laboratory investigations, erythrocyte sedimentation rate (ESR), chest X-ray, microbiological investigations (including, direct microscopy examination, isolation and identification of mycobacterium TB, and testing sensitivity for anti-TB drugs).

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Results: MDR and XDR TB were more common among TB patients with persistent positive sputum despite anti TB treatment than newly diagnosed cases. Diabetes mellitus (DM), HIV and anemia were considered to be other risk factors for MDR-TB and XDR-TB. Management of MDR-TB and XDR TB is a challenge which should be undertaken by experienced clinicians at centers equipped with reliable laboratory service for mycobacterial culture and in vitro sensitivity testing as it requires prolonged use of expensive second-line drugs with a significant potential for toxicity.

Conclusion: Emergence of MDR-TB and XDR TB has the potential to be a serious public health problem in Egypt and that strengthened TB control and improved monitoring of therapy is needed.

Introduction

Tuberculosis has been present in humans since antiquity. Tubercular decay has been found in the spines of mummies from 3000 to 2400 BC. Phthisis is a Greek term for TB; Around 460 BC, Hippocrates identified phthisis as the most widespread disease of the times involving coughing up blood and fever, which was almost always fatal [1]. The bacillus causing TB, was identified and described on 24 March 1882 by Robert Koch. He received the Nobel Prize in physiology and medicine in 1905 for this discovery [1]. Koch did not believe that bovine and human TB were similar, which delayed the recognition of infected milk as a source of infection. Later, this source was eliminated by the pasteurization process. Koch announced a glycerin extract of the tubercle bacilli as a remedy for TB in 1890, calling it ''tuberculin''. It was not effective, but was later adapted as a test for pre symptomatic TB [1].

Early diagnosis and immediate initiation of treatment are essential for an effective TB control program. Delay in diagnosis is significant to both disease prognosis at the individual level and transmission within the community. Most transmissions occur between the onset of cough and initiation of treatment [2]. The diagnosis of pulmonary TB depends on clinical suspicion, response to treatment, chest radiographs, staining for acid fast bacilli (AFB), culture for TB, and, nucleic acid amplification (NAA) assays [2].

Despite many advances in the diagnosis of TB in recent years, sputum smear testing using the Ziehl–Nielsen stain (ZN) is still the basic tool for TB diagnosis and monitoring because it is a quick, simple, and low cost test that can be reproduced in any setting and used to detect infectious cases in the community, a task that constitutes the cornerstone of TB diagnosis and monitoring [3].

Although culture has always been considered to be the gold standard technique for the diagnosis of TB, the result may be negative in some smear-positive patients owing to the loss of viability of the bacilli or the process used to decontaminate the sample. Likewise, false positive results may arise because of contamination of specimens in the laboratory. Despite these limitations, culture still plays a key role in the diagnosis and management of TB [4].

Anti TB treatment has two main objectives. First, there is a need to rapidly kill those AFB living extracellular in lung cavities, which are metabolically active and are dividing continuously; this is required in order to attain the negativization of sputum and therefore to prevent further transmission of the disease. Second, it is necessary to achieve complete sterilization and elimination of those AFB replicating less actively in acidic and anoxic closed lesions, and to kill semi dormant AFB living intracellular in other host tissues, otherwise these bacilli may persist and will be responsible for subsequent TB relapses. These reasons, along with the prevention of drug resistance, support the use of a combination therapy for the treatment of TB [5].

Several risk factors have been identified in the causation of drug resistant TB, of which the three most important are previous treatment with anti-TB drugs which may be inappropriate, incomplete or erratic, high prevalence of drug resistant TB in the community and contact with a patient known to have drug resistant TB. In patients with previous treatment or disease, the odds of resistant TB were 4–7 times higher than for persons with no history of past treatment. However, standardized short course chemotherapy carries only a minimal risk of emergence of MDR-TB [6]. Other factors that may be responsible for increased risk of resistant TB are: co-infection with HIV, socioeconomically deprived groups in slums, prisons, correctional facilities, day care centers, intravenous drug abusers and other immunocompromised states as in transplant recipients, anti-cancer therapy patients, and patients with DM. Radio logically far advanced pulmonary TB patients with cavitary lesions were 4 times as likely to harbor drug resistant organisms [6].

Multidrug-resistant tuberculosis is defined as infection caused by mycobacterium TB resistant to isoniazid and rifampin. EDR- TB was defined initially as infection caused by mycobacterium TB not only resistant to isoniazid and rifampin but also to at least 3 of the 6 classes of second-line agents approved for the treatment of TB (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and para-aminosalicyclic acid) [7]. The World Health Organization (WHO) Global Task Force on XDR-TB modified the definition in October 2006 following the report of the outbreak in KwaZulu Natal. Because drug susceptibility testing is reliable only for amikacin, kanamycin, capreomycin, and fluoroquinolones among the second-line agents, the definition of EDR-TB is now resistance to isoniazid and rifampin in addition to resistance to any fluoroquinolone and any of the second-line injectable drugs: amikacin, kanamycin, and capreomycin [8].

The primary aim in the control of MDR-TB is to prevent its development in the first place. This can be done by Directly Observed Treatment Short Course (DOTS), which is the most cost effective way of treatment and prevention of MDR-TB.