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IMPORTANCE OF CATALASE ENZYME IN VIRULENCE OF ISONIAZID RESISTANT STRAINS OF *MYCOBACTERIUM TUBERCULOSIS* IN GUINEA-PIGS

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ABSTRACT

In this study, twenty-five strains of *Mycobacterium tuberculosis* resistant to isoniazid (INH) were isolated from patients with tuberculosis (TB). Nine strains (36%) were found to be virulent in guinea-pigs [root index virulence (RIV)>1]. The remaining sixteen strains (64%) were non-virulent (RIV<1). Of the nine strains resistant to INH as well as virulent to guinea-pigs, eight of them were found to be catalase positive and only one strain was catalase negative, whereas the remaining sixteen INH resistant strains were catalase negative. A strong association was observed between INH resistance and catalase positivity and virulence ($p<0.0001$; chi-square test). This study supports the hypothesis that catalase has an important role in the virulence of INH-resistant strains of *M. tuberculosis*.
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INTRODUCTION

Isoniazid (INH) is a synthetic antibiotic which appears to have several targets within the mycobacterial cell. INH requires MTB catalase peroxidase enzyme for its activity.[9] The relationship between catalase activity in INH-resistant MTB and virulence has been a controversial issue for several decades.[8] Middlebrook and Cohn reported for the first time that INH-resistant strains of MTB isolated from patients with tuberculosis were non-virulent in guinea-pigs. They proposed that lack of virulence was due to reduced catalase activity.[5-6] This observation was later confirmed by Selkon and coworkers.[8] Transformation of *M. tuberculosis* with wild-type *kat*-G by Zhang et al. restored INH susceptibility and virulence to resistant isolates.[13-14]

The aim of this study was to reinvestigate the importance of catalase activity in the virulence of INH resistant strains of MTB in guinea-pigs.

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MATERIALS AND METHODS

Twenty-five strains of MTB resistant to INH were isolated from patients at the Massih Daneshvari Hospital, Tehran, most of which were immigrated Afghans. All isolates were identified by biochemical tests such as niacin, nitrate reduction, arylsulfate and semiquantitative catalase reaction. Eight strains (32%) were catalase positive and the remaining seventeen strains (68%) were catalase negative. Twenty-five MTB strains sensitive to INH as well as catalase positive were selected as the control group.

Seventy-five pathogen-free female Hartley strain guinea-pigs weighing 400-600g were obtained from Razi Institute, Tehran. All animals were randomly allocated to cages for treatment and control groups prior to injection. The animals were kept and allowed a two-week adjustment period prior to infection. The animals were tested for tuberculin reaction and only tuberculin negative animals were selected and labelled by tattooing their ears.

Colonies of MTB were freshly harvested from two weeks-old Lowenstein Jensen (L.J.) medium and were diluted to yield a suspension containing 2×10^6 cfu/mL. 75 animals were randomly chosen and injected with 25 strains