Study to determine presence of resistance to second-line anti-tuberculosis drugs in Kenyan isolates.

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

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DEDICATION

I dedicate this research project to my parents Givan Saya and Margaret Saya and to my sisters and brother; it's been a tough journey, but with your constant re-assurance, I have come this far.

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LIST OF ABBREVIATIONS AND ACRONYMS

AFB	acid-fast bacilli
$BaCl_2$	Barium chloride
CDC	United States Center for Disease Control and Prevention
CFU	colony forming units
CRDR	Centre for Respiratory Diseases Research
DNA	Deoxyribonucleic Acid
DOT	Directly Observed Therapy
DST	Drug Susceptibility Testing
GLC	Gas Liquid Chromatography
HPLC	High Performance Liquid Chromatography
ITROMID	Institute of Tropical Medicine and Infectious Diseases
IUATLD	International Union Against Tuberculosis and Lung Disease
JKUAT	Jomo Kenyatta University of Agriculture and Technology
KEMRI	Kenya Medical Research Institute
LJ	Lowenstein-Jensen
M	Molar concentration
MAC	*Mycobacterium avium* complex
MDR-TB	Multi Drug Resistant Tuberculosis
MGIT	Mycobacterial Growth Indicator Tube
MOTT	Mycobacteria other than tubercle bacilli

MTB	*Mycobacterium tuberculosis*
N/A	Not Applicable
NTM	Non-tuberculous mycobacteria
PCR	Polymerase Chain Reaction
PNB	p-nitro benzoic acid
RNA	Ribonucleic acid
RR	Resistant Ratio
SLDs	Second-line drugs
TCH	Thiophen-2-carboxylic acid hydrazide
TB	Tuberculosis
WHO	World Health Organization
XDR	Extensively Drug Resistant
ZN	Ziehl-Neelsen

ABSTRACT

Tuberculosis (TB) is yet far from being controlled. Despite the fact that several reasons could be attributed to this, a significant contributing factor is the development of resistance to the currently available drugs due to the successful adaptation of the pathogen to these drugs. Second-line anti-TB drugs are being used for treatment of Multi-Drug Resistant TB (MDR-TB) patients.

The purpose of this study was to investigate the presence of drug resistant strains of *Mycobacterium tuberculosis* (MTB) to second-line anti-TB drugs (SLDs) in first-line predetermined drug susceptibility isolates obtained from different studies carried out at the Centre for Respiratory Diseases Research (CRDR) between 2002 and 2007.

A total of 216 MTB isolates including 78 first-line drug resistant isolates to individual and combined drugs and 138 first-line drugs susceptible isolates to all drugs were selected for this study. Of the 78 first-line resistant isolates, 25 isolates were MDR-TB strains. Resistant ratio and proportion methods were used to test. All the isolates were tested for susceptibility to four second-line drugs including cycloserine, gatifloxacin, ethionamide and kanamycin. Using S.P.S.S. computer data analysis programme, analysis of data was done using chi-square to compare resistance and susceptibility among the drugs, and to compare resistance and susceptibility between the first-line susceptible and resistant isolates to second-line anti-TB drugs.

Of the 216 first-line isolates tested, 96.3% were sensitive, 2.2% were fully resistant and 1.5% had intermediate resistance. Of the 78 isolates tested, 94.9% were sensitive, 4.2% were fully resistant and 1% were intermediate resistant. Of the 138 isolates tested, 97.1% were sensitive, 1.1% were fully resistant and 1.8% were intermediate resistant. Drug resistance to second-line anti-TB drugs was not statistically associated with previous first-line anti-TB drugs resistance, although the resistance level of second-line anti-TB drugs in the first-line resistant isolates was higher than in the first-line sensitive isolates.

Resistance of MTB to second-line anti-TB drugs is present in Kenya. There was resistance to all the four second-line anti-TB drugs tested in this study, in both first-line resistant and sensitive isolates. There was no XDR-TB strain isolated.

As resistant MTB increases in Kenya further studies are needed to evaluate second-line DST techniques and establish an appropriate one within the national policies. Since the samples used in this study may not be a representation of the current national status of drug resistance to second-line anti-TB drugs, a national surveillance is important to establish the prevalence of second-line anti-TB drugs resistance in the country.