

**EVALUATION OF DIRECT NITRATE REDUCTASE ASSAY FOR
CULTURE AND SUSCEPTIBILITY TESTING OF
MYCOBACTERIUM TUBERCULOSIS TO FOUR PRIMARY ANTI-
TUBERCULAR DRUGS**

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by

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ABSTRACT

Rapid, simple drug susceptibility tests applicable in developing countries would allow earlier treatment of patients with multi-drug resistant *Mycobacterium tuberculosis* infections. To evaluate the performance and feasibility of a Direct Nitrate Reductase Assay for detecting the drug-resistant tuberculosis directly in microscopy-positive samples, this prospective study comparing the sensitivity and specificity of the Direct Nitrate Reductase Assay with the gold standard Lowenstein Jensen proportion method was carried out at National TB and SAARC TB and HIV/AIDS Centre, Thimi, Bhaktapur, Nepal from June 2008 to March 2009. Out of 302 sputum samples taken, 144 (47.68%) sputum samples those showing positive for Acid Fast Bacilli were tested by Direct Nitrate Reductase Assay method and the test was completed on 121 (84%) specimens. Of the 23 specimen for which the test was not completed, 12 (8.33%) were culture-negative and 11 (7.63%) were contaminated on culture. The sensitivity and specificity of the Direct Nitrate Reductase Assay were studied in 121 specimens and were 100% and 91% for isoniazid, 100% and 98.95% for rifampicin, 96% and 91.66% for streptomycin, and 100% and 98% for ethambutol respectively. Of the 121 samples tested for drug susceptibility, 72.72% (88) were sensitive to all four drugs and 27.28% (33) were resistant to one or more drugs with 19% (23) multi-drug resistant. The Direct Nitrate Reductase Assay is sensitive and specific enough for the detection of multi-drug resistant tuberculosis and is also easy to perform, rapid and inexpensive, making it suitable for developing countries. However, its usefulness for national drug resistance surveys should be assessed.

Key words: sensitivity, specificity, gold standard, multi-drug resistant

TABLE OF CONTENTS

	Page no.
Title Page	i
Recommendation	ii
Certificate of Approval	iii
Board of Examiners	iv
Acknowledgement	v
Abstract	vi
Table of Contents	vii
List of Abbreviations	xiii
List of Tables	xv
List of Photographs	xvi
List of Appendices	

CHAPTER I: INTRODUCTION

CHAPTER II: OBJECTIVES

4

2.1 General objective

2.2 Specific objective

CHAPTER III: LITERATURE REVIEW

5-41

3.1 Mycobacteria

3.1.1 Morphological characteristics

3.1.2 Cell wall structure

3.1.3 Genomic structure

3.1.4 Cultural characteristics

3.1.5 Culture media for isolation of Mycobacteria

- 3.1.6 Susceptibility to physical and chemical agents
- 3.1.7 Pathogenesis
 - 3.1.7.1 Mode of infection
 - 3.1.7.2 Predisposing factors
 - 3.1.7.3 Virulence factors
 - 3.1.7.4 Mechanism of infection
- 3.2 Tuberculosis
- 3.3 Epidemiology of tuberculosis
 - 3.3.1 Global situation of TB
 - 3.3.2 Situation of TB in Asia
 - 3.3.3 Situation of TB in SAARC region
 - 3.3.4 Situation of TB in Nepal
- 3.4 Types of tuberculosis
 - 3.4.1 Pulmonary tuberculosis
 - 3.4.2 Extra-pulmonary tuberculosis
- 3.5 Clinical diagnosis of pulmonary tuberculosis
- 3.6 Radiological diagnosis of pulmonary tuberculosis
- 3.7 Serological diagnosis of pulmonary tuberculosis
- 3.8 Tuberculin skin testing
- 3.9 Laboratory diagnosis of pulmonary tuberculosis
 - 3.9.1 Specimen collection and transport
 - 3.9.2 Macroscopic examination
 - 3.9.3 Microscopic examination
 - 3.9.4 Processing of sputum specimen
 - 3.9.5 Culture of sputum specimen
 - 3.9.6 Identification of isolates
 - 3.9.6.1 Growth on medium containing PNB
 - 3.9.6.2 Niacin test
 - 3.9.6.3 Nitrate reductase test
 - 3.9.6.4 Catalase test

- 3.9.6.5 Urease test
- 3.9.6.6 Pyrazinamidase test
- 3.9.6.7 Thiophen-2-Carboxylic acid Hydrazide susceptibility test
- 3.9.6.8 Molecular techniques for identification of Mycobacterium
- 3.9.7 Antimicrobial susceptibility testing of Mycobacteria
- 3.10 Methods of detection of drug resistance
 - 3.10.1 Conventional phenotypic methods
 - 3.10.1.1 Proportion method
 - 3.10.1.2 Resistance ratio method
 - 3.10.1.3 Absolute concentration method
 - 3.10.1.4 BACTEC radiometric method
 - 3.10.1.5 Mycobacterial Growth Indicator Tube Method
 - 3.10.2 Genotypic methods
 - 3.10.2.1 Desoxyribonucleic acid (DNA) sequencing
 - 3.10.2.2 Solid-phase hybridization techniques
 - 3.10.2.3 Real-time PCR techniques
 - 3.10.2.4 Microarrays
 - 3.10.3 Colorimetric methods
 - 3.10.4 Nitrate reductase assay method
- 3.11 Treatment of tuberculosis
 - 3.11.1 Anti-tuberculous drugs
 - 3.11.2 Notification of cases
 - 3.11.3 Treatment regimens
 - 3.11.4 Treatment categories
 - 3.11.5 Adverse effects of anti-TB drugs
- 3.12 Drug resistant tuberculosis
 - 3.12.1 Types of drug resistance
 - 3.12.2 Factors associated with drug resistance
 - 3.12.3 Mechanism of resistance
 - 3.12.4 MDR-TB: Multi-drug TB

3.12.5 XDR-TB: Extensive drug resistant TB

CHAPTER IV: MATERIALS AND METHODS

4.1 Materials	47
4.2 Study setting	
4.3 Study design	
4.4 Study population	
4.5 Study period	
4.6 Data collection	
4.7 Laboratory methodology	
4.7.1 Collection of sputum sample	48
4.7.2 Evaluation of sputum	48
4.7.3 Macroscopic examination of sputum	
4.7.4 Processing of sputum specimen	
4.7.5 Microscopic examination of processed sputum	
4.7.6. Direct nitrate reductase assay method	
4.7.6.1. Inoculation and incubation	
4.7.6.2 Interpretation of results	
4.7.7 Conventional Lowenstein-Jensen method	
4.7.7.1 Inoculation and incubation	
4.7.7.2 Culture examination	
4.7.7.3 Recording and reporting of culture results	
4.7.7.4 Microscopic examination by ZN-staining	
4.7.8 Identification of isolates	
4.7.8.1 Inoculum preparation	
4.7.8.2 Growth on medium containing p-nitrobenzoic acid (PNB)	
4.7.9 Antimicrobial susceptibility testing	53
4.7.9.1 Preparation of drug containing media	53
4.7.9.2 Preparation of bacillary suspension	

4.7.9.3 Dilution of bacillary suspension for inoculation	
4.7.9.4 Inoculation and incubation	
4.7.9.5 Interpretation of results	
4.7.10 Quality control	
4.8 Data analysis	
CHAPTER V: RESULTS	55-62
5.1 Case and gender-wise distribution of PTB patients enrolled in the study	
5.2 Age and gender-wise distribution of patients PTB included in the study	
5.3 AFB smear positivity among cases	57
5.4 Culture-positivity among cases	58
5.5 Correlation between microscopy and culture	59
5.6 Growth pattern of culture positive samples on LJ medium containing PNB	59
5.7 Age and gender-wise distribution of culture positive specimen	60
5.8 Drug Susceptibility Pattern of culture positive isolates	60
CHAPTER VI: DISCUSSION AND CONCLUSION	63-67
6.1 Discussion	63
6.2 Conclusion	67
CHAPTER VII: SUMMARY AND RECOMMENDATIONS	68-70
7.1 Summary	68
7.2 Recommendations	70
REFERENCES	71-79
APPENDICES: I-IX	i-xi

LIST OF ABBREVIATIONS

AFB	Acid Fast Bacilli
AIDS	Acquired Immuno Deficiency Syndrome
AST	Antimicrobial Susceptibility Testing
BACTEC	Becton Dickinson and Company
BCG	Bacilli Calmette Guéruin
CDC	Centre for Disease Control
CMI	Cell Mediated Immunity
DOTS	Directly Observed Treatment Short course
DST	Drug Susceptibility Test
EMB/E	Ethambutol
GLC	Gas Liquid Chromatography
HIV	Human Immunodeficiency Virus
HPLC	High Performance Liquid Chromatography
ICT	Immuno Chromatographic Technique
IFN	Interferon
IL	Inter-Leukin
INH/H	Isoniazid
IS	Insertion Sequence
IUATLD	International Union Against Tuberculosis and Lung Diseases
LAMs	Lipoarabinomannans
LCR	Ligase Chain Reaction
LJ media	Lowenstein Jensen media
MDR	Multi Drug Resistant
MDR-TB	Multi Drug Resistant-Tuberculosis
MGIT	Mycobacterium Growth Indicator Tube
MIC	Minimum Inhibitory Concentration
MOTT	Mycobacteria Other than Tuberculous bacilli

MTC	Mycobacterium Tuberculosis Complex
NALC-NaOH	N-Acetyl L-Cysteine-Sodium Hydroxide
NRA	Nitrate Reductase Assay
NTC	National Tuberculosis Centre
NTM	Non-Tuberculous Mycobacteria
NTP	National Tuberculosis Programme
PCR	Polymerase Chain Reaction
PNB	Para-NitroBenzoic acid
PPD	Purified Protein Derivative
PTB	Pulmonary Tuberculosis
PZA/Z	Pyrazinamide
RFLP	Restriction Fragment Length Polymorphism
RFP/R	Rifampicin
SAARC	South Asian Association for Regional Cooperation
SEAR	South East Asia Region
SM/S	Streptomycin
STC	SAARC Tuberculosis Centre
TB	Tuberculosis
TCH	Thiophen-2-Carboxylic acid Hydrazide
TNF	Tumor Necrosis Factor
WHO	World Health Organization
XDR	Extended Drug Resistant
ZN staining	Ziehl-Neelsen staining
Z-TSP	Zephiran-Tri-Sodium Phosphate

LIST OF TABLES

- Table 3.1: Macroscopic examination of sputum sample (Cheesbrough, 2002)
- Table 3.2: Reporting of sputum smear by ZN staining method (WHO, 1998)
- Table 3.3: Reporting of culture on LJ medium (WHO, 1998)
- Table 3.4: Critical concentration of main antibiotics in the proportion method ($\mu\text{g/ml}$)
- Table 3.5: Recommended treatment regimens for each treatment category (WHO, 1997)
- Table 4.1: Critical concentrations of primary anti-tubercular drugs used in the study
- Table 5.1: Case and gender-wise distribution of PTB patients enrolled in the study
- Table 5.2: Age and gender-wise distribution of the PTB patients included in the study
- Table 5.3: Results of AFB smear by microscopy
- Table 5.4: Results of sputum culture
- Table 5.5: Results of microscopy and culture of sputum specimen.
- Table 5.6: Results of culture positive isolates on LJ medium containing PNB
- Table 5.7: Age and Gender-wise distribution of smear and culture-positive cases
- Table 5.8: Drug Susceptibility Pattern of culture positive isolates determined by the
Proportion method and Direct NRA method.
- Table 5.9: Comparison of Direct NRA results with Proportion method
- Table 5.10: Resistance profiles of *M. tuberculosis* isolates (n = 121).

LIST OF PHOTOGRAPHS

Photograph 1: Culture of *Mycobacterium tuberculosis* in Lowenstein-Jensen medium

Photograph 2: Result of drug susceptibility test by direct nitrate reductase assay method
(all drug susceptible *Mycobacterium tuberculosis*)

Photograph 3: Result of drug susceptibility test by direct nitrate reductase assay method
(isoniazid and streptomycin resistant)

Photograph 4: Drug susceptibility testing of isolated strain in LJ-media by proportion
method

Photograph 5: Drug susceptibility testing of H₃₇R_v strain in LJ-media by proportion
method

LIST OF APPENDICES

	Page no.
APPENDIX-I: Questionnaire	i
APPENDIX-II: Material used during the study	ii
APPENDIX-III: Composition and preparation of reagents	iii
1. Z-N Staining reagent	iii
2. Digestion and decontamination reagent	iii
3. Griess reagent	iv
4. Mc Farland no. 1	iv
APPENDIX-IV: Preparation of culture media	v
1. Lowenstein-Jensen (LJ) medium	
2. Preparation of 0.5 mg/ml para-nitrobenzoic acid (PNB) containing media	v
3. Preparation of drug solutions and drug containing media	vi
4. Preparation of media for Nitrate Reductase Assay (NRA)	vii
APPENDIX-V: 1. Ziehl-Neelsen (ZN) staining procedures	viii
2. Sodium hydroxide (Modified Petroff) method for digestion and decontamination of sputum sample	viii
APPENDIX-VI: Identification of <i>Mycobacterium tuberculosis</i>	ix
APPENDIX-VII: Quality check of media for drug susceptibility test	ix
APPENDIX-VIII: Calculation of Specificity, Sensitivity and Predictive Value	x
APPENDIX-IX: Statistical Analysis	xi

