

**COMPARISON OF THE RESISTANCE RATIO AND  
PROPORTION METHODS FOR DRUG SUSCEPTIBILITY  
TESTING OF *Mycobacterium tuberculosis* ISOLATED FROM  
PATIENTS VISITING NATIONAL TUBERCULOSIS CENTRE**

A

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Master of Science in Microbiology  
(Medical)

by

**Sushma Acharya**

Central Department of Microbiology  
Tribhuvan University  
Kirtipur, Kathmandu, Nepal

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## RECOMMENDATION

This is to certify that Ms. Sushma Acharya has worked under our supervision and guidance on the thesis entitled “**Comparison of the resistance ratio and proportion methods for drug susceptibility testing of *Mycobacterium tuberculosis* isolated from patients visiting National Tuberculosis Centre**” as a partial fulfillment of M.Sc. Degree in Microbiology. To the best of our knowledge this is an original research work of her and has not been submitted for any other degree.

---

Dr. Prakash Ghimire, Ph.D.

Associate Professor

Central Department of Microbiology

Tribhuvan University

Kirtipur, Kathmandu

Nepal

---

Mr. Dhruba Kumar Khadka

Sr. Medical Technologist (Microbiologist)

National Tuberculosis Centre

Thimi

Bhaktapur

Nepal

Date: \_\_\_\_\_

## **CERTIFICATE OF APPROVAL**

On the recommendation of Associate Professor **Dr. Prakash Ghimire, Ph.D.** and **Mr. Dhruva Kumar Khadka** this dissertation work by **Ms. Sushma Acharya**, entitled **“Comparison of the resistance ratio and proportion methods for drug susceptibility testing of *Mycobacterium tuberculosis* isolated from patients visiting National Tuberculosis Centre”** has been approved for the examination and is submitted to Tribhuvan University in partial fulfillment of the requirement for M.Sc. Degree in Microbiology.

---

**Dr. Anjana Singh**

Head of Department

Central Department of Microbiology

Tribhuvan University

Kirtipur, Kathmandu

Nepal

Date: \_\_\_\_\_

## BOARD OF EXAMINERS

**Recommended by:**

---

Dr. Prakash Ghimire, Ph.D.  
(Supervisor)

---

Mr. Dhruva Kumar Khadka  
(Supervisor)

**Approved by:**

---

Dr. Anjana Singh, Ph.D.  
Head of Department

**Examined by:**

---

Dr. Dwij Raj Bhatta, Ph.D.  
(Internal Examiner)

---

Dr. Basista Rijal, Ph.D.  
(External Examiner)

Date: \_\_\_\_\_

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**Sushma Acharya**

## ABSTRACT

This CDM TU & NTC collaborative study was carried out based at National Tuberculosis Centre (NTC), Thimi, Bhaktapur, Nepal from September 2006 to June 2007 with an objective to compare the two *in vitro* methods (viz, resistance ratio (RR) and proportion (PR) methods), used to determine antimicrobial susceptibilities of *Mycobacterium tuberculosis* against primary anti-tubercular drugs {Isoniazid (INH), Rifampicin (RFP), Streptomycin (SM) and Ethambutol (EMB)}.

Among 221 isolates of *M. tuberculosis* analyzed during the study period, 56.56% and 57.47 % of the isolates were resistant to at least one drug by resistance ratio and proportion method respectively. Among all resistant isolates detected, 5.88% were resistance to INH, 4.52% to SM and 1.81% to RFP by RR method, while 5.43% were resistance to both INH and SM and 0.45% to RFP by PR method. No EMB resistant isolates could be detected by both methods. Multi-drug resistance (MDR) was observed in 28.96% and 29.86% isolates by RR and PR methods respectively.

On correlation analysis using Mc Nemar chi-square test, no significant difference between the two tests were observed ( $p > 0.05$ ). The results showed high agreement between both the methods and agreement rates to INH, RFP, SM and EMB were 93.21, 93.67, 93.21 and 94.12 % respectively. Similarly, the agreement rates between both the methods using kappa analysis showed kappa value of 0.864, 0.854, 0.861 and 0.838 for INH, RFP, SM and EMB respectively, which is believed to be good agreement between both methods ( $k = 0.80$  to  $1.00$  :very good agreement).

Thus both the resistance ratio and proportion methods are equally good for determining drug susceptibility of *M. tuberculosis*, so that we need not to depend only on tedious method like proportional method for Antimicrobial susceptibility testing.

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## **LIST OF ABBREVIATIONS**

AAFB	Acid and Alcohol Fast Bacilli
AFB	Acid Fast Bacilli
AIDS	Acquired Immuno Deficiency Syndrome
AMP	Adenosine Mono Phosphate
AST	Antimicrobial Susceptibility Testing
BACTEC	Becton Dickinson and Company
BCG	Bacille Calmette Guéruin
CDC	Centre for Disease Control
CMI	Cell Mediated Immunity
DNA	Deoxyribo Nucleic Acid
DOTS	Directly Observed Treatment Short course
DST	Drug Susceptibility Test
ELISA	Enzyme Linked Immuno Sorbet Assay
EMB/E	Ethambutol
E-test	Epsilometer-test
GI	Growth Index
HIV	Human Immunodeficiency Virus
INH/H	Isoniazid
IUATLD	International Union Against Tuberculosis and Lung Diseases
LAMs	Lipoarabinomannans
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 Cysteine-Sodium Hydroxide



NTC	National Tuberculosis Centre
NTM	Non-Tuberculous Mycobacteria
NTP	National Tuberculosis Programme
PCR	Polymerase Chain Reaction
PNB	Para-NitroBenzoic acid
PPD	Purified Protein Derivative
PR	Proportion method
PTB	Pulmonary Tuberculosis
PZA/Z	Pyrazinamide
RFP/R	Rifampicin
ROI	Reactive Oxygen Intermediate
RR	Resistance Ratio method
SAARC	South Asian Association for Regional Cooperation
SEAR	South East Asia Region
SM/S	Streptomycin
SPSS	Statistical Package for Social Science
STC	SAARC Tuberculosis Centre
T	Thioacetazone
TB	Tuberculosis
TNF	Tumor Necrosis Factor
Vs.	Versus
WHO	World Health Organization
XDR	Extended Drug Resistant
XDR-TB	Extended Drug Resistant Tuberculosis
ZN staining	Ziehl-Neelsen staining
Z-TSP	Zephiran-Tri-Sodium Phosphate

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