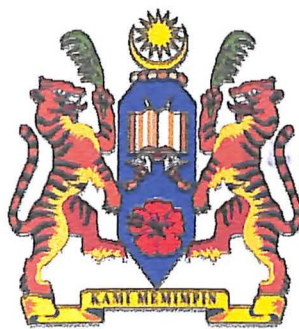


ASSESSING THE CHEST RADIOGRAPHIC SEVERITY OF
PULMONARY TUBERCULOSIS AMONG HIV AND NON-
HIV PATIENTS

By

DR. SANTHI VARATHARAJA PILLAI

Dissertation Submitted in Partial Fulfilment of the Requirements
for the Degree of Master of Medicine
(Radiology)



UNIVERSITI SAINS MALAYSIA

UNIVERSITI SAINS MALAYSIA
2008

To
my mum Mdm Sakunthala Pillai
and
my brother Mr Umasangar Pillai
a very special Thank You.

ACKNOWLEDGEMENT

The author would like to express her sincere gratitude to the following individuals for their valuable comments, guidance, support and co-operation that they have given during the preparation of this dissertation. Without them, this study would not have been successful.

- Special thanks goes to my supervisors, Dr Nik Munirah Nik Mahdi, lecturer and radiologist at Department of Radiology, Hospital Universiti Sains Malaysia, Kubang Kerian, and Dr Md. Ariff Bin Abas, AMP., Consultant radiologist and Head, Department of Diagnostic Imaging, Hospital Raja Perempuan Zainab II, Kota Bharu, who have given their effort, patience and full support throughout the period to make this study a success.
- Co-supervisor of this dissertation, Dr. Mahiran Mustafa, Consultant Physician & ID Specialist, Department of Medicine, Hospital Raja Perempuan Zainab II, Kota Bharu, whose support and help in giving ideas, guidance and solutions to all problems that occurred during the study.
- My gratitude goes to Dr Mohd Ezane Aziz, lecturer, radiologist and Head of Department of Radiology, Hospital Universiti Sains Malaysia, Kubang Kerian.
- My special gratitude goes to Dr Win Mar @ Salmah Jallaluddin and Dr Noreen Norfaraheen Lee Abdullah, (my lecturers and radiologists) for their presence, valuable advices and comforting words helped me along the way.
- My appreciation also goes to Dr Mohd Shafie Abdullah and Dr Juhara Harun, (lecturers and radiologists) who directly or indirectly contributed their ideas and comments.
- I have furthermore to thank Dr Muhammad Naeem Khan (Department of Biostatistics and Research Methodology), Dr Tengku Norbanee Tengku Hamzah

(Department of Biostatistic and Epidemiology), Dr Kamarul Imran Musa (Department of Community Medicine) and AP Dr Syed Hatim Noor @ Nyi Nyi Naing (Department of Biostatistic and Epidemiology) for their assistance in statistical analyses.

- Especially I am obliged to Dr Noor Azizah Binti Abdul Halim, Radiologist, Department of Diagnostic Imaging, Hospital Raja Perempuan Zainab II, Kota Bharu, for her assistance and support to complete this dissertation.
- I would particularly like to express my warmest gratitude to Mr Udin Abdullah (radiographer, formerly in the Department of Diagnostic Imaging, HRPZ-II) and Mdm Enikartini Daud (Guru Bahasa, Centre for Languages and Translation, USM) for their enthusiasm and helping me in Bahasa Malaysia (BM) translation.
- I would like to thank the staffs in the record office of chest clinic, microbiology laboratory and physician clinic in Hospital Raja Perempuan Zainab II, Kota Bharu for their ever willingness to trace the patient records, results and radiographs whenever required.
- Not forgetting, I am deeply indebted to my former radiologist and coordinator Dr Vijayalakshmi Krishnapillai, who is now Consultant Radiologist and Head, Department of Diagnostic Imaging in Hospital Tengku Ampuan Rahimah, Klang, for her everlasting encouragement, advice and guidance.
- Most of all to my brother Mr Umasangar Pillai and my mum Mdm Sakunthala Pillai for their endless encouragement, support and comforting words along the way, a very special Thank You.

TABLE OF CONTENTS

TABLE OF CONTENTS

CONTENTS	PAGE
<i>Title Page</i>	i
<i>Acknowledgement</i>	ii
<i>Table of Contents</i>	v
<i>List of Tables</i>	xi
<i>List of Figures</i>	xiii
<i>Abbreviations and Symbols</i>	xvi
<i>Abstract</i>	xix
<i>Bahasa Malaysia</i>	xx
<i>English</i>	xxiii
SECTION 1	1
1. INTRODUCTION	2
SECTION 2	4
2. LITERATURE REVIEW	5
2.1 GENERAL	5
2.2 EPIDEMIOLOGY	5
2.3 OVER-VIEWS ON THE PATHOGENESIS AND CLINICAL FEATURES OF PULMONARY TUBERCULOSIS	7

2.4 OVER-VIEWS ON THE PATHOGENESIS AND CLINICAL FEATURES OF TUBERCULOSIS IN HIV/AIDS	9
2.5 DIAGNOSIS OF THE PULMONARY TUBERCULOSIS	11
2.6 RADIOLOGICAL INVESTIGATION IN PULMONARY TUBERCULOSIS	12
2.7 BACTERIOLOGICAL EXAMINATION OF SPUTUM IN PTB	22
2.7.1 SPUTUM MICROSCOPY FOR ACID-FAST BACILLI (AFB) SMEAR	22
2.7.2 SPUTUM CULTURE FOR MYCOBACTERIA TUBERCULOSIS	25
2.8 INDICATION FOR SCREENING OF HIGH RISK GROUPS BASED ON MOH, MALAYSIA GUIDELINE	26
2.9 MOH GUIDELINES ON MANAGEMENT OF TUBERCULOSIS	26
SECTION 3	29
3. OBJECTIVES AND HYPOTHESIS	30
3.1 GENERAL OBJECTIVE	30
3.2 SPECIFIC OBJECTIVES	30
3.3 RESEARCH QUESTION	30
3.4 NULL HYPOTHESIS	30
SECTION 4	31
4. METHODOLOGY	32
4.1 RESEARCH DESIGN	32
4.2 POPULATION AND SAMPLE	32
4.3 OPERATIONAL DEFINITION	33
4.4 INCLUSION CRITERIA	35
4.5 EXCLUSION CRITERIA	35
4.6 SAMPLE SIZE	36
4.7 SAMPLING METHOD	37

4.8 DATA COLLECTION PROCEDURE	40
4.9 RESEARCH TOOL	41
4.10 MATERIALS AND METHODS	41
4.10.1 DIAGNOSIS OF TUBERCULOSIS	41
4.10.2 IMAGING PROTOCOL FOR CHEST RADIOGRAPH IN HRPZ-II	41
4.10.3 CHEST RADIOGRAPH REPORTING CRITERIA	42
4.10.4 SPUTUM FOR AFB SMEAR MICROSCOPY AND CULTURE MTB	46
4.10.5 BLOOD TEST FOR HIV STATUS	46
4.11 ETHICAL CONSIDERATION	47
4.12 STATISTICAL ANALYSIS	48
SECTION 5	49
5. RESULTS	50
5.1 PATIENTS CHARACTERISTICS	50
5.1.1 GENDER DISTRIBUTION	50
5.1.2 ETHNIC DISTRIBUTION	50
5.1.3 AGE DISTRIBUTION	50
5.1.4 SMOKING	51
5.1.5 CLOSE CONTACT WITH TUBERCULOSIS	51
5.1.6 CLINICAL SYMPTOMS AND SIGNS OF PTB	53
5.1.7 LABORATORY SPUTUM EXAMINATION FINDING AMONG NON-HIV AND HIV PATIENTS.	54
5.2 STATISTICAL ANALYSIS	55
5.2.1 CHEST RADIOGRAPH FINDINGS AMONG NON-HIV AND HIV PATIENTS.	55
5.2.2 VARIABLE CHEST RADIOGRAPH APPEARANCES	57

SECTION 6	76
6. DISCUSSION	77
6.1 GENERAL	77
6.2 PATIENTS CHARACTERISTICS	77
6.2.1 GENDER DISTRIBUTION	77
6.2.2 ETHNIC DISTRIBUTION	78
6.2.3 AGE DISTRIBUTION	78
6.2.4 SMOKING	79
6.2.5 CLOSE CONTACT WITH TB	80
6.2.6 CLINICAL SYMPTOMS AND SIGNS OF PTB	80
6.2.7 LABORATORY SPUTUM EXAMINATION FINDING AMONG NON-HIV AND HIV PATIENTS	82
6.3 STATISTICAL ANALYSIS	84
6.3.1 CHEST RADIOGRAPH FINDINGS AMONG NON-HIV AND HIV PATIENTS	84
6.3.2 VARIABLE CHEST RADIOGRAPHS APPEARANCE	86
6.3.3 IMPORTANCE OF CLINICAL ASSESSMENT IN PTB	90
6.3.4 IMPLICATION OF RESULT	92
SECTION 7	95
7. CONCLUSION	96
SECTION 8	97
8. LIMITATION AND RECOMMENDATION	98
8.1 LIMITATION OF THE STUDY	98
8.2 RECOMMENDATION	99

SECTION 9	101
9. REFERENCES	102
SECTION 10	108
10. APPENDIX	109
10.1 CONSENT	109
10.2 DATA SHEET	120
10.2.1 DATA ENTRY SHEET (Filled by Clinician)	120
10.2.2 DATA COLLECTION SHEET (Filled by Reporting Radiologist)	121
10.2.3 DATA COLLECTION SHEET (Filled by Researcher)	123
10.3 ILLUSTRATIONS	124

LIST OF TABLES

LIST OF TABLES

TABLES	PAGE
TABLE 1: Manifestations of Tuberculosis Activity in the Chest Radiograph	20
TABLE 2: Quantitation Scale for Sputum Acid-Fast Bacillus Smears (IUAT SCALE)	24
TABLE 3: Standard Antituberculosis Drugs and the Recommended Dosages	27
TABLE 4: Chest Radiograph Classification of PTB	43
TABLE 5: Descriptive Analysis between Non-HIV and HIV groups	52
TABLE 6: Clinical Signs and Symptoms of Tuberculosis among Non-HIV and HIV Patients	53
TABLE 7: Pre-treatment Laboratory Sputum Examination Findings in Non-HIV and HIV Patient	54
TABLE 8: Pre-treatment Chest Radiograph Findings between Non-HIV and HIV Patients	55
TABLE 9: Pre-treatment Chest Radiograph Appearances between Non-HIV and HIV Patients	55
TABLE 10: Six Months Post-treatment Chest Radiograph Findings between Non-HIV and HIV Patients	56
TABLE 11: Six Months Post-treatment Chest Radiograph Appearances between Non-HIV and HIV Patients	56
TABLE 12: Variable Chest Radiograph Appearance of Pulmonary Tuberculosis among Non-HIV and HIV Patients	57

LIST OF FIGURES

LIST OF FIGURES

FIGURES	PAGE
FIGURE 1: Flow Chart - Recommended by MOH, 24weeks/6months Treatment Regimen (Adult)	28
FIGURE 2: Methodology Flow Chart	40
FIGURE 3: Histogram - Age Distribution among Non-HIV and HIV Patients	51
FIGURE 4: Tuberculoma	58
FIGURE 5: Cavitation	59
FIGURE 6: Pleural effusion	60
FIGURE 7: Hilar adenopathy	61
FIGURE 8: Pneumothorax	62
FIGURE 9: Miliary TB	63
FIGURE 10: Fibrosis and Bronchiectasis and Pleural thickening	64
FIGURE 11: Lung fibrosis and apical Pleural thickening	65
FIGURE 12: Cicatrization atelectasis	66
FIGURE 13: Nodules	67
FIGURE 14: Consolidation	68
FIGURE 15: Normal	69
FIGURE 16: Mildly Abnormal Pre-treatment Chest Radiograph	70
FIGURE 17: Moderately Abnormal Pre-treatment Chest Radiograph	71
FIGURE 18: Severely Abnormal Pre-treatment Chest Radiograph	72
FIGURE 19: Mildly Abnormal Post-treatment Chest Radiograph	73
FIGURE 20: Moderately Abnormal Post-treatment Chest Radiograph	74
FIGURE 21: Severely Abnormal Post-treatment Chest Radiograph	75

FIGURE 22: Mildly Abnormal (minimal)	124
FIGURE 23: Moderately Abnormal (moderately advanced)	125
FIGURE 24: Severely Abnormal (far advanced)	126

ABBREVIATIONS
AND
SYMBOLS

ABBREVIATIONS AND SYMBOL

ABBREVIATIONS

AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
CDC	Centre for Disease Control
CXR	Chest Radiograph
C/S	Culture and Sensitivity
D/S	Direct Smear
FNAC	Fine Needle Aspiration Cytology
IU	International Tuberculin Units
HIV	Human Immunodeficiency Virus
HRPZ-II	Hospital Raja Perempuan Zainab-II
HUSM	Hospital Universiti Sains Malaysia
MKAK	Makmal Kesihatan Awam Kebangsaan
MTB	Mycobacterium tuberculosis
M.Tuberculosis	Mycobacterium tuberculosis
Non-HIV	Non Human Immunodeficiency Virus
NTBC	National Tuberculosis Centre
PCR	Polymerase Chain Reaction
PA	Posteroanterior
PPD	Purified Protein Derivative of Tuberculosis
PTB	Pulmonary Tuberculosis
TB	Tuberculosis
TU	Tuberculin Unit
WHO	World Health Organisation

SYMBOLS

n	number of samples
=	equal to
vs.	versus
i.e.	that is
e.g.	example
x	times (multiply by)
kVp	kilovoltage peak (x-ray tube voltage)
mAs	milliamperes seconds (tube current)
6/12	six months
'05	2005
'08	2008
>	more than
<	less than
&	and

ABSTRACT

ABSTRAK

Pengenalan

Tuberkulosis paru-paru (PTB) merupakan satu penyakit berjangkit yang paling lazim berlaku di negara-negara membangun dan komplikasi penyakit ini merupakan satu cabaran dan amat sukar didiagnos. Kadar tuberkulosis di kalangan pesakit yang mempunyai daya pertahanan badan lemah adalah sangat tinggi dan ia juga merupakan antara penyumbang utama kepada morbiditi dan mortaliti.

Objektif

Tujuan utama kajian ini adalah untuk menentukan perhubungan di antara tahap keparahan radiograf dada pada pesakit PTB dengan status HIV (bukan HIV dan HIV). Kajian ini juga bertujuan untuk menilai perbezaan dalam pelbagai manifestasi radiograf dada yang berbeza di kalangan pengidap PTB bagi dua kumpulan kajian seperti yang dinyatakan di atas.

Bahan dan Kaedah

Kajian ini berbentuk retrospektif, yang mana ia memfokus kepada pesakit PTB di kalangan dewasa yang dijangkiti dan tidak dijangkiti HIV di Hospital Raja Perempuan Zainab-II, Kota Bharu. Pesakit-pesakit yang dipilih untuk kajian ini adalah pesakit yang mempunyai simptom dan tanda-tanda PTB, yang telah disahkan melalui “sputum smear AFB” atau dengan kultur MTB.

KEPUTUSAN

Kadar umur untuk pesakit bukan HIV adalah 46.5 tahun dan untuk pesakit dengan HIV ialah 32.6 tahun. Analisa menunjukkan 93% pesakit bukan HIV dan 94% pesakit HIV pula menunjukkan keputusan radiograf dada yang tidak normal semasa fasa pra-perawatan. Keputusan radiograf dada yang dijalankan selepas enam bulan perawatan dijalankan didapati menunjukkan 18% pesakit bukan HIV dan 31% pesakit HIV mempunyai radiograf dada yang kembali normal. Kajian statistik bagi kedua-dua kumpulan ini didapati tidak mempunyai perbezaan signifikan dari segi tahap keparahan (“severity”) radiograf dada pada pesakit PTB semasa fasa pra-perawatan (p -value=0.668) dan selepas perawatan (p -value=0.135). Perbandingan yang dibuat antara dua kumpulan kajian semasa pra-perawatan menunjukkan pesakit HIV dengan PTB lebih kerap menghidapi “pleural effusion” (23% vs. 14%, p -value=0.081) dan “miliari tuberculosis” (7% vs. 3%, p -value=0.196) walaupun tidak signifikan. Pembesaran kelenjar “hilar/mediastinal lymphadenopathy” (32% vs. 4%, p -value<0.001) pula menunjukkan perubahan yang signifikan di kalangan kumpulan pesakit yang disahkan HIV. Manakala pesakit bukan HIV pula lebih ramai mempunyai “pleural thickening” (36% vs. 11%, p -value<0.001), “bronchiectasis” (16% vs. 5%, p -value=0.007) dan “fibrosis” paru paru (41% vs. 17%, p -value<0.001). Perubahan radiograf dada yang menunjukkan “cavitation” (33% vs 24%, p -value=0.177) pula lebih rendah di kalangan kumpulan pesakit HIV tetapi ianya tidak menunjukkan perbezaan yang signifikan antara dua kumpulan kajian ini.

KESIMPULAN

Kajian statistik bagi kedua-dua kumpulan yang dikaji mendapati tidak mempunyai perbezaan signifikan dari segi tahap keparahan (severity) radiograf dada pada pesakit

mengidap PTB semasa fasa pra-perawatan ($p\text{-value}=0.668$) dan selepas perawatan ($p\text{-value}=0.135$). Kajian ini juga terdapat perbezaan yang signifikan secara statistik di antara pesakit PTB yang dijangiti HIV semasa fasa selepas enam bulan perawatan dengan menunjukkan lebih banyak bilangan radiografi dada yang normal. Pesakit PTB yang mengidap HIV juga mempunyai perbezaan yang ketara pada radiograf dada terutamanya dalam manifestasi nodul limfa (lymphadenopathy) “hilar and mediastinum”. Sementara itu “pleural thickening”, “bronchiectasis”, “fibrosis” dan “consolidation” pula lebih kerap pada pesakit bukan HIV.

ABSTRACT

INTRODUCTION

Pulmonary tuberculosis (PTB) is the most common infectious disease in developing countries and the development of complications remains a difficult diagnostic challenge. The proportion of tuberculosis developing in the immunocompromised hosts is especially high and is one of the leading causes of morbidity and mortality.

OBJECTIVE

The main purpose of this study was to determine the association between the chest radiograph severity of pulmonary tuberculosis with HIV status (non-HIV and HIV). This study also evaluated the differences in the various chest radiograph appearances of pulmonary tuberculosis among the above mentioned two study groups.

MATERIALS AND METHODS

This was a retrospective study, focused on adult pulmonary tuberculosis patients with non-HIV and HIV coinfection from Hospital Raja Perempuan Zainab-II, Kota Bharu. Those patients who had clinical symptoms and signs of PTB with either sputum smear AFB or culture MTB proven pulmonary tuberculosis were recruited for this study.

RESULT

Mean age of the patients in both non-HIV and HIV groups were 46.5 and 32.6 respectively. Ninety three percent (93%) of non-HIV and 94% of HIV patients demonstrated abnormal chest radiograph during pre-treatment phase. Whereas the chest radiograph done six months after the commencement of treatment demonstrated 18%

and 31% of normal finding in non-HIV and HIV patients, respectively. There was no significant statistical difference found among these two study groups in the chest radiograph severity/extent of PTB during pre-treatment (p-value=0.668) and post-treatment (p-value=0.135) phases. Comparison of the two groups showed HIV patients with PTB had higher incidence of pleural effusion (23% vs. 14%, p-value=0.081) and miliary tuberculosis (7% vs. 3%, p-value=0.196), even-though non-significant. Nevertheless, hilar/mediastinal lymphadenopathy (32% vs. 4%, p-value<0.001) demonstrated significant difference in the HIV group. Whereas in non-HIV patients more of pleural thickening (36% vs. 11%, p-value<0.001), bronchiectasis (16% vs. 5%, p-value=0.007) and lung fibrosis (41% vs. 17%, p-value<0.001) were demonstrated. Lesser incidence of chest radiograph presentation with cavitation (33% vs. 24%, p-value=0.177) found in the HIV group, however no significant statistical difference among the two study groups.

CONCLUSION

There was no significant statistical difference found among the two study groups in the chest radiograph severity of PTB during pre-treatment (p-value=0.668) and (p-value=0.135) post-treatment phases. This study also demonstrated significant statistical difference among the PTB with HIV co-infected patients by showing more number of normal chest radiograph in the post-treatment phase. HIV with PTB coinfecting patient had considerable differences in the various chest radiograph presentations specifically with hilar/mediastinal lymphadenopathy. While pleural thickening, bronchiectasis, fibrosis and consolidation found more commonly in non-HIV patients.