



**MAKERERE**

**UNIVERSITY**

**ABDOMINAL SONOGRAPHIC CHANGES AMONG HIV-TB CO-  
INFECTED ADULT PATIENTS INITIATING HIGHLY  
ACTIVE ANTIRETROVIRAL THERAPY  
AT MULAGO HOSPITAL COMPLEX**

**BY**

**JABO CHRISTIAN ROY THOMAS**

**MBChB (MUST)**

**SUPERVISORS**

**DR. KISEMBO HARRIET**

**MBChB, MMED, MPH (CONSULTANT RADIOLOGIST)**

**MULAGO NATIONAL REFERRAL AND TEACHING HOSPITAL**

**DR. WORODRIA WILLIAM**

**MBChB, MMED, PhD (SENIOR CONSULTANT PHYSICIAN)**

**MULAGO NATIONAL REFERRAL AND TEACHING HOSPITAL**

**DR. BUGEZA SAMUEL**

**MBChB, MMED (RADIOLOGIST)**

**LECTURER MAKERERE UNIVERSITY**

**COLLEGE OF HEALTH SCIENCES (SCHOOL OF MEDICINE)**

**A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT  
FOR THE AWARD OF THE DEGREE OF MASTER  
OF MEDICINE IN RADIOLOGY  
OF MAKERERE UNIVERSITY**

**MARCH 2014**

## **DECLARATION**

I, JABO CHRISTIAN ROY THOMAS declare that the work presented in this dissertation is original and has not been presented for any award in any other University.

Contributions made by other people towards this research have been acknowledged and appreciated.

**SIGNATURE:** .....

**DR JABO CHRISTIAN ROY THOMAS.**

**2010/HD11/1068U**

**DATE:** .....

## APPROVAL

This study dissertation entitled, “*Abdominal Sonographic Changes among HIV-TB Co-Infected Adult Patients Initiating Highly Active Antiretroviral Therapy at Mulago Hospital Complex*” has been submitted to Makerere University for examination with our approval as supervisors.

1. DR. KISEMBO HARRIET

MBChB, MMED, MPH (Consultant Radiologist)

Mulago National Referral and Teaching Hospital

Signature .....

Date.....

2. DR. WORODRIA WILLIAM

MBChB, MMED, PhD (Senior Consultant Physician)

Mulago National Referral and Teaching Hospital

Signature .....

Date.....

3. DR. BUGEZA SAMUEL

MBChB, MMED (Radiologist)

Lecturer, Makerere University

College Of health Sciences (School Of Medicine)

Signature .....

Date.....

## **DEDICATION**

This work is dedicated to the entire Jabo family for their love, prayers, encouragement and support towards my education.

## **ACKNOWLEDGEMENT**

I wish to express my sincere gratitude to the Almighty God for his unending love and continuous providence.

I am forever grateful to the Infectious Disease Institute for the sponsorship towards the completion of my dissertation.

Sincere thanks go to my supervisors: Dr. Kisembo Harriet, Dr Worodria William and Dr Bugeza Samuel for the valuable guidance given towards this dissertation and all the lecturers in the Department of Radiology for their contribution towards my post graduate education.

I extend my utmost gratitude to the Board of Governors and administration of Mengo Hospital Kampala for the sponsorship towards my postgraduate training.

To Mr. Kuniha Sam, I am forever grateful for the abdominal ultrasound scanning techniques I acquired from him during the training which enabled me to perform the research.

Lastly, special thanks to Dr. Mugisha Julius Sebikali, my brother, friend and colleague who challenged me academically through discussions and practical sessions and kept me company during our struggle to achieve excellence.

# TABLE OF CONTENTS

<b>DECLARATION.....</b>	<b>i</b>
<b>APPROVAL .....</b>	<b>ii</b>
<b>DEDICATION.....</b>	<b>iii</b>
<b>ACKNOWLEDGEMENT.....</b>	<b>iv</b>
<b>LIST OF FIGURES .....</b>	<b>ix</b>
<b>LIST OF TABLES .....</b>	<b>x</b>
<b>OPERATIONAL DEFINITIONS .....</b>	<b>xi</b>
<b>LIST OF ABBREVIATIONS .....</b>	<b>xiii</b>
<b>ABSTRACT.....</b>	<b>xiv</b>
<b>CHAPTER ONE: INTRODUCTION.....</b>	<b>1</b>
1.1 Background of the Study .....	1
1.2 Problem statement.....	3
1.3 Justification.....	4
1.4 Research question .....	4
1.5 Null hypothesis .....	4
1.6 General objective .....	5
1.7 Specific objectives .....	5
<b>CHAPTER TWO: LITERATURE REVIEW.....</b>	<b>6</b>
2.1 Introduction.....	6
2.2 Abdominal sonographic features of TB.....	6
2.3 Abdominal sonographic findings in HIV infection. ....	6
2.4 Abdominal ultrasound findings in relation to follow up on treatment for tuberculosis.....	7
2.5 Tuberculosis Immune Reconstitution Inflammatory Syndrome. ....	8
<b>CHAPTER THREE: METHODOLOGY .....</b>	<b>10</b>
3.1 Study design.....	10
3.2 Study settings .....	10

3.3 Study population .....	11
3.4 Target population .....	11
3.5 Inclusion criteria .....	11
3.6 Exclusion criteria .....	11
3.7 Sample size estimation.....	11
3.8 Study procedure .....	12
3.9 Study variables:.....	12
3.10 Equipment and other requirements .....	13
3.11 Technique.....	13
3.12 Data collection .....	14
3.13 Data management and analysis.....	14
3.14 Quality control .....	14
3.15 Ethical consideration.....	14
3.16 Dissemination of results.....	15
<b>CHAPTER FOUR: PRESENTATION AND FINDINGS OF THE STUDY .....</b>	<b>16</b>
4.1 Results.....	16
4.2 Socio - demographic characteristics .....	17
4.2.1 Distribution of patients by sex .....	17
4.2.2 Age distribution of study participants.....	17
4.3 Tribe and Occupation.....	18
4.3.1 Occupation distribution of the patients .....	18
4.4 Clinical features. ....	18
4.5 Sonographic findings at base line ultrasound scan. ....	19
4.6 Abdominal sonographic findings.....	20
4.6.1 Baseline, scheduled and unscheduled scan abdominal sonographic findings. ....	20
4.6.2 Changes in ultrasound findings on follow up scans.....	21
4.6.4 Liver findings.....	21
4.6.5 Splenic findings .....	22
4.6.6 Peritoneal fluid (Ascites) .....	22
4.6.7 Bowel thickening .....	22

4.6.8 Renal findings .....	23
4.6.9 Gall bladder findings.....	23
4.6.10 Appendicular findings.....	23
4.6.11 Prostatic findings .....	23
4.7 Abdominal sonographic findings on ultrasound.....	24
4.8 Clinical features and worsening of radiological findings. ....	31
4.9 Relating the clinical symptoms to the abdominal sonographic changes.....	32
4.9.1 Relating the clinical symptoms to improvement or worsening of the abdominal sonographic changes .....	33
4.10 Determining if the null hypothesis is true.....	33
<b>CHAPTER FIVE: DISCUSSION.....</b>	<b>34</b>
5.1 Discussion.....	34
5.1.1 Abdominal sonographic findings among HIV-TB co-infected adult patients initiating HAART at Mulago Hospital Complex. ....	35
5.1.2 Lymphadenopathy.....	35
5.1.3 Liver findings.....	36
5.1.4 Splenic findings .....	37
5.1.5 Kidney findings.....	38
5.1.6 Bowel thickening .....	39
5.1.7 Peritoneal fluid.....	39
5.1.8 Gall bladder disease .....	40
5.1.9 Appendicular findings.....	41
5.1.10 Pelvic findings .....	41
5.2 Relating clinical symptoms to presence or absence of abdominal sonographic changes ...	41
5.2.1 Relating clinical symptoms to whether changes were better or worse: .....	42
5.3 Determining if the null hypothesis is true among the follow up patients. ....	43
5.4 Study limitations .....	43



<b>CHAPTER SIX: CONCLUSION AND RECOMMENDATION.....</b>	<b>44</b>
6.1 Conclusions.....	44
6.2 Recommendations.....	44
<b>APPENDIX 1A: Study Consent Form – In English .....</b>	<b>45</b>
<b>APPENDIX 1B: Study Consent Form – in Luganda.....</b>	<b>47</b>
<b>APPENDIX II: Questionnaire .....</b>	<b>50</b>
<b>REFERENCES.....</b>	<b>53</b>

## LIST OF FIGURES

Figure 4.1: Flow diagram of HIV-TB co-infected adult patients initiating HAART at Mulago Hospital Complex .....	16
Figure 4.2 Sex distribution of HIV-TB co-infected adult patients initiating HAART at Mulago Hospital Complex. ....	17
Figure 4.3: Age distribution of HIV-TB co-infected adult patients initiating HAART at Mulago Hospital Complex. ....	17
Figure 4.4: Graph comparing occurrence of clinical symptoms at baseline and on follow up scans .....	18
Figure 4.5: Sonographic findings at baseline scan.....	19
Figure 4.6(a) enlarged lymph node at baseline. ....	24
Figure 4.6(b) enlarged lymph node at unscheduled visit.....	24
Figure 4.7(a) hypoechoic splenic lesion at baseline .....	24
Figure 4.7(b) regression of hypoechoic lesion on scheduled scan.....	25
Figure 4.8 (a) Splenic abscess seen at baseline.....	25
Figure 4.8(b) regression of splenic abscess seen at scheduled scan .....	26
Figure 4.8(c) shows a baseline longitudinal sonogram in a 24 year old male with miliary TB. ..	26
Figure 4.9 (a) free ascites seen at baseline scan.....	27
Figure 4.9(b) loculated ascites seen at unscheduled scan. ....	27
Figure 4.10 Small bowel wall thickening seen at scheduled scan .....	28
Figure 4.11 (a) Double layer wall appearance of gall bladder seen at baseline.....	28
Figure 4.11 (b) Gall bladder wall thickening seen at scheduled scan.....	29
Figure 4.11(c) Thickened double layer gall bladder wall at unscheduled scan .....	29
Figure 4.12 Appendicitis seen at baseline scan .....	30
Figure 4.13: Prostatic abscess seen at unscheduled scan .....	30

## LIST OF TABLES

Table 4.1: Comparing abdominal sonographic findings at baseline and follow up scans .....	20
Table 4.2: Changes on follow up scans .....	21
Table 4.3: Clinical features and worsening of radiological findings on follow up scans. ....	31
Table 4.4: Bivariate analysis relating clinical symptoms to presence or absence of sonographic changes.....	32
Table 4.5: Multivariate analysis relating clinical symptoms to presence or absence of a sonographic change.....	32
Table 4.6: Bivariate analysis relating clinical symptoms to better or worse sonographic changes. ....	33
Table 4.7: Determining if the null hypothesis is true among the follow up patients.....	33

## **OPERATIONAL DEFINITIONS**

**TUBERCULOSIS:** An infectious disease of humans and animals caused by the tubercle bacillus and characterized by the formation of tubercles on the lungs and other tissues of the body, often developing long after the initial infection.

**HIV:** A lentivirus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome.

**TB-HIV CO-INFECTION:** Simultaneous infection by TB and HIV.

**ABDOMINAL TB:** TB affecting the peritoneum, abdominal lymph nodes, omentum, liver, spleen, and/or gastrointestinal tract.

**PARADOXICAL TB IRIS:** Manifestation of new or recurrent TB symptoms or signs in patients being treated for TB during early antiretroviral therapy (ART).

**HAART:** Combined antiretroviral treatment regimens (three or more different ART drugs) used to suppress HIV viral replication and the progression of HIV disease..

**EARLY INITIATION OF HAART IN HIV-TB CO-INFECTION:** Starting ARVs within 2 weeks of initiating TB treatment.

**ULTRASOUND:** Mechanical radiant energy with a frequency greater than 20KHZ (cycles per second).Diagnostic ultrasound uses a frequency 1MHZ-20MHZ.

**SONOGRAPHIC:** Pertaining to or comprising the ultrasound evaluation of an organ.

**ECHOGENICITY:** Intensity of echo reflected by tissue or structures from inside the body.

**HYPERECHOIC:** Refers to high intensity echo compared to an adjacent structure.

**HYPOECHOIC:** Refers to low intensity echo compared to an adjacent structure.

**ASCITES:** Accumulation of fluid in the peritoneal cavity.

**LYMPHADENOPATHY:** A disease or enlargement of lymph nodes.

**HEPATOMEGALY:** Enlargement of the liver.

**SPLENOMEGALY:** Enlargement of the spleen.

**NEPHROPATHY:** Damage to or disease of a kidney

**ABSCESS:** A collection of pus that has accumulated within a tissue because of an inflammatory process in response to either an infectious process or other foreign materials.

**HEMANGIOMA:** A benign and usually self-involuting tumor of the endothelial cell that line blood vessels, and is characterized by increased number of normal or abnormal vessels filled with blood.

**CHOLECYSTITIS:** Inflammation of the gall bladder.

**APPENDICITIS:** Inflammation of the appendix.

**PROSTATITIS:** Inflammation of the prostate gland.

## LIST OF ABBREVIATIONS

<b>AIDS</b>	:	Acquired immune deficiency syndrome
<b>HIV</b>	:	Human immunodeficiency virus
<b>TB</b>	:	Tuberculosis
<b>IRIS</b>	:	Immune reconstitution inflammatory syndrome
<b>TBIRIS</b>	:	Tuberculosis immune reconstitution inflammatory syndrome
<b>HAART</b>	:	Highly Active Anti Retroviral Therapy
<b>ART</b>	:	Anti Retroviral Therapy
<b>INSHI</b>	:	International Network for the Study of HIV-associated IRIS
<b>MTB</b>	:	Mycobacterium tuberculosis
<b>WHO</b>	:	World Health Organization
<b>ATB</b>	:	Abdominal tuberculosis
<b>ZN</b>	:	Ziehl Nielsen
<b>ESR</b>	:	Erythrocyte sedimentation rate
<b>CRP</b>	:	C reactive protein
<b>ALT</b>	:	Alanine transaminase
<b>AST</b>	:	Aspartate transaminase
<b>HIVAN</b>	:	Human immunodeficiency virus associated nephropathy
<b>OR</b>	:	Odds ratio

## **ABSTRACT**

Human immunodeficiency virus (HIV) infection increases the risk for infection with *Mycobacterium tuberculosis* (TB). In HIV-TB co-infected patients, abdominal tuberculosis accounts for 11-16% of extra pulmonary cases. Abdominal sonographic changes following initiation of Highly Active Antiretroviral Therapy (HAART) in these patients may be due to the response to anti-Tuberculous drugs and HAART, due to adverse reactions to these treatments or due to other associated co-morbidities. The changes may show improvement of abdominal features during treatment or worsening as a result of paradoxical TB-IRIS. They may also be new findings due to other opportunistic infections. Ultrasound imaging is a useful auxiliary investigative modality in the management of HIV-TB co-infected patients initiating HAART and it can demonstrate these abdominal sonographic changes. However, there is no recent research on its role in the management of HIV-TB co-infection in Uganda.

### **Objective**

The study aimed at describing the abdominal sonographic findings among HIV-TB co-infected adult patients initiating HAART at Mulago Hospital Complex.

### **Methodology**

A prospective descriptive study design was used. This study was nested in a prospective observational cohort study whose aim was to determine the incidence and predictors of clinical and immunological outcomes in adult patients co-infected with TB-HIV. It was conducted in the Department of Radiology at Mulago Hospital, the national referral hospital. Adults with HIV-TB co infection eligible for HAART were enrolled in the study. Serial abdominal ultrasound scans using low frequency (2-5MHZ) and high frequency probes (7-12MHZ) were performed. Data were collected on structured questionnaires, entered into a computer using Epi data version 3.1 and analysed using Stata version 11 with the help of a statistician.

### **Results**

Eighty nine patients were enrolled and had a baseline ultrasound scan, 70 (78.7%) patients had a scheduled follow up scan and 10 (11.2%) had an ultrasound scan during an unscheduled visit. 9 patients (10.1%) were lost to follow up of whom 6 patients died (66.7%)

while 3 (33.3%) did not return for the scheduled scan. 65.2% were males and 34.8 % were females giving a male to female ratio of 1.9:1. The age range was from 20-62 years and the median age was 32 years.

There was no statistically significant difference in the abdominal sonographic findings at base line and 4 weeks after initiating HAART. Clinical features of abdominal pain and abdominal distention were significantly associated with development of abdominal sonographic changes while abdominal pain was the only symptom significantly associated with worsening of the abdominal sonographic changes (a OR=6.0, 95% CI=1.106-13.552 and a p value=0.038) on follow up or on development of symptoms of TB-IRIS.

Fourteen patients had normal abdominal scans while 75 had features suggestive of abdominal TB on baseline scan like lymphadenopathy, hepatosplenomegaly and splenic nodules. Fourteen patients had features suggestive of TB-IRIS on the follow up and unscheduled scans. Co-morbidities like nephropathy, splenic candidiasis and cavernous hemangiomas were diagnosed.

Sonographic changes observed in the abdomen were resolution of splenic infarction, regression of splenic abscesses, appendicitis, prostatic abscess, ascites, lymphadenopathy, cholecystitis, splenomegaly and hepatomegaly.

## **Conclusions**

There is an increased incidence of HIV-TB co-infected patients with sonographic features which may be suggestive of abdominal tuberculosis at baseline scan.

Worsening abdominal sonographic changes within 4 weeks of initiating HAART tend to be associated with paradoxical TB-IRIS.

Abdominal pain and distention are associated with development of abdominal sonographic changes.

Abdominal pain is significantly associated with worsening of abdominal sonographic features on follow up visits.



There is no statistically significant difference between abdominal sonographic features at baseline and follow up 4 weeks after initiating HAART.

### **Recommendations**

A study designed to establish the clinico-sonographic-pathological correlation and the schedule for follow up scans is highly recommended.

Follow up abdominal sonography should be delayed beyond 4 weeks unless patients develop new symptoms or worsened symptoms.

A screening ultrasound examination for TB-IRIS should be performed in all HIV-TB co-infected on treatment who develop abdominal pain.