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# Impact of Highly Active Anti-Retroviral Therapy on paediatric Human Immuno-Deficiency Virus associated left ventricular dysfunction within the Johannesburg teaching hospital complex

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# UNIVERSITY OF THE WITWATERSRAND

## IMPACT OF HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY ON PAEDIATRIC HUMAN IMMUNO-DEFICIENCY VIRUS ASSOCIATED LEFT VENTRICULAR DYSFUNCTION WITHIN THE JOHANNESBURG TEACHING HOSPITAL COMPLEX

**Lungile Pepeta**

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree

**MASTER OF MEDICINE (MMED.)**

(PAEDIATRICS AND CHILD HEALTH)

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Johannesburg, South Africa, 2012

DECLARATION

I, Lungile Pepeta hereby declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Paediatrics and Child Health in the University of Witwatersrand, Johannesburg and has not been submitted for any other degree at this or any other university.

Signature

L Pepeta

Date 11/09/2012

Place JOHANNESBURG

## DEDICATION

To my wife Noluvuyo, our daughter Kungawo and my brothers Lunga and Samkeliso.

To my nephew Lusanda.

To the memories of my mother Nondyebo, my father Richard and my sister Nelisiswe. May their souls rest in peace.

## Presentations arising from this research

This work was presented at the Ninth Congress of the South African Heart Association in the Wild Coast Sun, Eastern Cape, South Africa, 2-5 November 2008 and the Fifth World Congress in Cardiac and Cardiothoracic Surgery, Cairns, Queensland Province, Australia, 21-26 June 2009.

## Publication arising from this research

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## Abstract

BACKGROUND

Cardiovascular disease is a common complication of advanced HIV disease in both paediatric and adult patient groups and may present with left ventricular (LV) dysfunction. Introduction of Highly Active Antiretroviral Therapy (HAART) has improved outcomes in patients presenting with LV dysfunction. However, mitochondrial toxicity, a complication of HAART, may present with myocardial dysfunction.

OBJECTIVE

The aim of the study was to analyze the outcome of paediatric patients with left ventricular dysfunction placed on Highly Active Anti-Retroviral Therapy.

METHOD

Retrospective review of records of HIV positive children with LV dysfunction managed at a Johannesburg Teaching Hospital Complex. Demographic data was collected and other variables such as echocardiographic assessment of fractional shortening (FS), CD4 percentage, viral load and nutritional status were compared before and after commencement of HAART.

RESULTS

Thirty four patients with LV dysfunction had their records reviewed.

Eighteen patients with LV dysfunction received HAART (group 1), while the remaining 16 patients were HAART naïve and managed in the pre HAART era (group 2). The median age of group 1 at their initial visit was 94 months and the male to female ratio was 1:1. Seventeen

of the 18 patients showed improved LV function on treatment with an increase of median FS from 17% to 33.5% ($p < 0.0001$). The initial median FS in group 2 was 13%, which increased to 19% with follow up ($p = 0.07$). Other notable improvements on treatment in group 1 was the increase in the CD4 percentage from a median of 12% to 30.5% ($p < 0.0001$), viral load suppression from an initial median viral logarithm of 5.4 $Log_{10}$ to undetectable levels (<400copies/ml) ($p < 0.0001$) and significant recovery of nutritional status. The median weight-for-age z-scores in the group 1 patients progressed from -1.70 pre-HAART to -1.32 with follow up ($p = 0.0083$). The group 2 patients had similar z-scores at the initial visit, with a median of -2.47. Follow up weight-for-age z-scores were available in only five out of the 16 patients, median of -3.37 ($p = 0.089$).

CONCLUSION

The findings are in keeping with other reports showing an improvement in left ventricular function in patients with HIV associated cardiomyopathy treated with HAART. The recovery of myocardial function is associated with improvement of their initially poor immunological and nutritional status.

## ACKNOWLEDGEMENTS

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## List of Abbreviations

| | |
|---|---|
| AIDS | Acquired Immuno-deficiency Syndrome |
| ARV | Anti-retroviral drug |
| Aspirin | Acetylsalicylic Acid |
| CDC | Centre for Disease Control |
| DNA | Deoxyribonucleic Acid |
| EBV | Ebstein Barr Virus |
| FS | Fractional Shortening |
| HAART | Highly Active Anti-retroviral Therapy |
| HIV | Human Immuno-deficiency Virus |
| HIV-1 | Human Immuno-deficiency Virus Type 1 |
| IL | Interleukin |
| LV | Left Ventricular |
| MAP | Mitogen Activated Protein |
| mtDNA | Mitochondrial Deoxyribonucleic Acid |
| NNRTI | Non-Nucleoside Reverse Transcriptase Inhibitor |
| NRTI | Nucleoside Reverse Transcriptase Inhibitor |

| | |
|---|---|
| PCR | Polymerase Chain Reaction |
| PI | Protease Inhibitor |
| PBMC | Peripheral Blood Mononuclear Cell |
| RNA | Ribonucleic Acid |
| TGF | Transforming Growth Factor |
| TNF | Tumour Necrosis Factor |

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## Glossary

**Immune Status:** CD4 percentage was used as an indicator of immune competence. The percentage compared to the actual CD4 count is a more reliable measure in children. By definition a CD4 percentage of >25% indicates immune competence; 15%-24% indicates moderate immunosuppression; and less than 15% indicates severe immunosuppression.[86]

**Highly Active Anti-Retroviral Therapy (HAART):** An antiretroviral drug combination of three or more drugs capable of reducing the viral load to undetectable levels (<400 copies/ml).[86]**(APPENDIX 1)**

**HIV infection Status:** The detection of Human Immunodeficiency Virus Deoxyribonucleic Acid using Polymerase Chain Reaction (HIV DNA PCR) in patients less than eighteen months, or detection of HIV antibodies using Enzyme-linked Immunosorbent Assay (HIV ELISA) in patients more than eighteen months of age.[86]

**Left ventricular dysfunction:** Left ventricular fractional shortening of less than twenty five percent (25%).[87,88]

**Nutritional Status**: The weight-for-age and height-for-age z-scores were used to compare the nutritional status pre- and during HAART.[49] Malnutrition (Poor Nutritional Status) was defined as weight-for-age z-scores less than -1 SD and more than -2SD for mild malnutrition, less than -2SD and more than -3SD for moderate malnutrition and less than -3SD for severe malnutrion.

**Outcome:** Recorded as death, lost to follow up (presumed dead), alive with LV dysfunction, or alive without LV dysfunction.

**Viral load:** A measure of HIV Ribonucleic Acid (HIV RNA) copies detected in patient's serum.

Undetectable levels were defined as being less than 400 copies/ml.