A cohort of children with HIV in Papua New Guinea during an era of anti- retroviral transition

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The AIDS Pandemic

- HIV is a persistent public health concern with a high burden globally; children and young adults are especially affected

Global estimates for children (<15 years) | 2021

Children living with HIV	**1.7 million**	[1.3 million–2.1 million]
New HIV infections in 2021	**160 000**	[110 000–230 000]
Deaths due to AIDS in 2021	**98 000**	[67 000–140 000]

UNAIDS epidemiological survey 2022

Paediatric HIV in PNG

Paediatric Hospital Reporting: 11th Annual PHR 2020

- Overall Case Fatality Rate (2019-2020) 17%

Port Moresby General Hospital – 2020 Annual Report

- Total number of Admission 90
- Total Deaths 30
- Case Fatality Rate 33%
- Total Paediatric Admission -2094 5%

- *Highest mortality seen in HIV apart from cancer, SAM and Meningitis, PNA*

National Health Department Report 2020

Paediatric HIV in PNG

- WHO rolled out dolutegravir *(DTG)* regimen in LMICs as a first-line ART treatment in 2016. In November 2020, the US FDA approved the 10mg dispersible tabs to use for children <20kg.

- New DTG regimen for children has been rolled out in PNG since 2020 as first- line ART for children.

- PMGH sees 15-20 infected children daily at the HIV clinic. There has been an increase in the admissions with OI's and with malnutrition or with complications of ART.

- The study was done at a critical time of transition of ART; the older regimes seemed to be failing, to new therapies that include DTG and LPV/r regime.

Aim of the study

- To determine the incidence of ART treatment failure in children living with HIV at Port Moresby General Hospital

- To record the difference in the clinical and virological outcomes for children from the original ART usually the NNRTI based agents, to the new dolutegravir (DTG) and lopinavir/ ritonavir (LPV/r) regimes

Methods

- **Study site:** PMGH Well Baby Clinic
- **Procedure:** A survey form was filled for those children recruited and it included each patient's demographics, nutritional information, assessment on clinical features of immune deficiency on each child, evidence of TB co- infection, the previous ART regimen the patient was on and for how long and viral loads pre and post ART change
- **Inclusive criteria:** Infants and children <18 years that have been on ART >6 months
- **Analysis:** Data entered into Excel spreadsheet and analyzed using Stata Version 16
- **Ethical Issues:** Clearance from the PMGH management and the UPNG SMHS Academic Board

Definitions of treatment failure (WHO)

- Clinical failure

❖ *New or current clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4) excluding TB after 6 months of effective ART*

- Immunological failure

❖ *<5 years: persistent CD4 levels <200 cells/mm3*

❖ *>5 years: persistent CD4 levels <100 cells/ mm3*

- Virological failure

❖ *Viral load >1000 copies/ml, provided patient compliant to ART and EAC been given, >6 months after being on ART*

Results

- 60 patients aged from 2 months to 18 years were recruited between October 2021 and July 2022 at the well baby clinic.

- Median age of diagnosis of HIV is 14.5 months *(IQR 7-36 months)*; median age of ART commencement is 17.5 months *(IQR 9- 36 months)*.

Table 1. *Demographic and clinical information at baseline*

Age in months: median (IQR)	**131 (98- 169) months**
Mother on ART: number (%)	46 (76.7%)
Father on ART: number (%)	33 (55%)
Nutrition	
Weight in kg: median (IQR)	23 (13- 34) kg
Height in cm: median (IQR)	128 (98- 133) cm
MUAC: median (IQR)	15 (13- 16) cm
Co- infection with tuberculosis: number (%)	**10 (16.7%)**
Co- trimoxazole prophylaxis: number (%)	**54 (90%)**
TB preventative therapy prophylaxis: number (%)	**2 (3.3%)**

Baseline

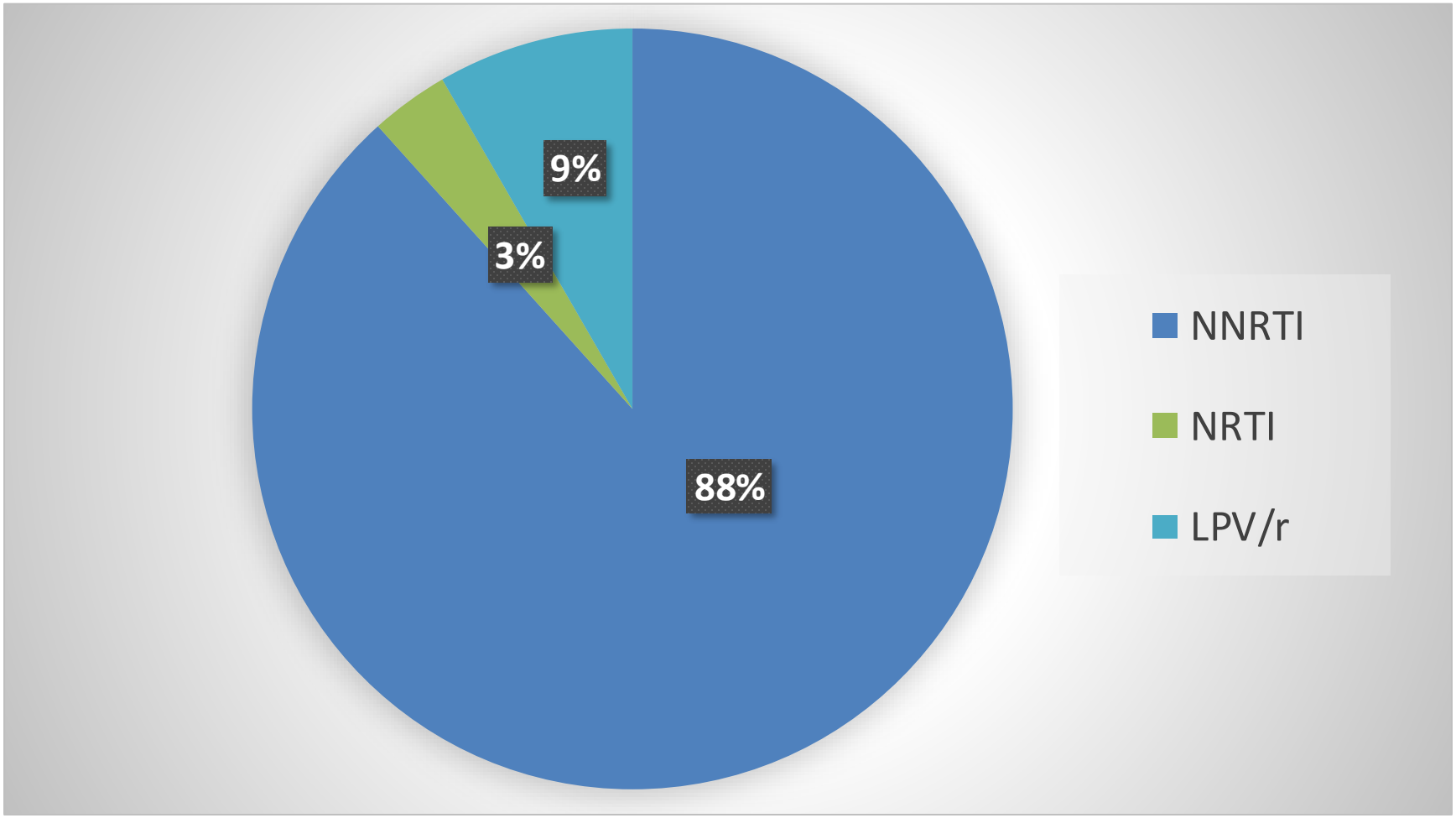


Figure 1: *The old ART regimes the children were on*

Baseline

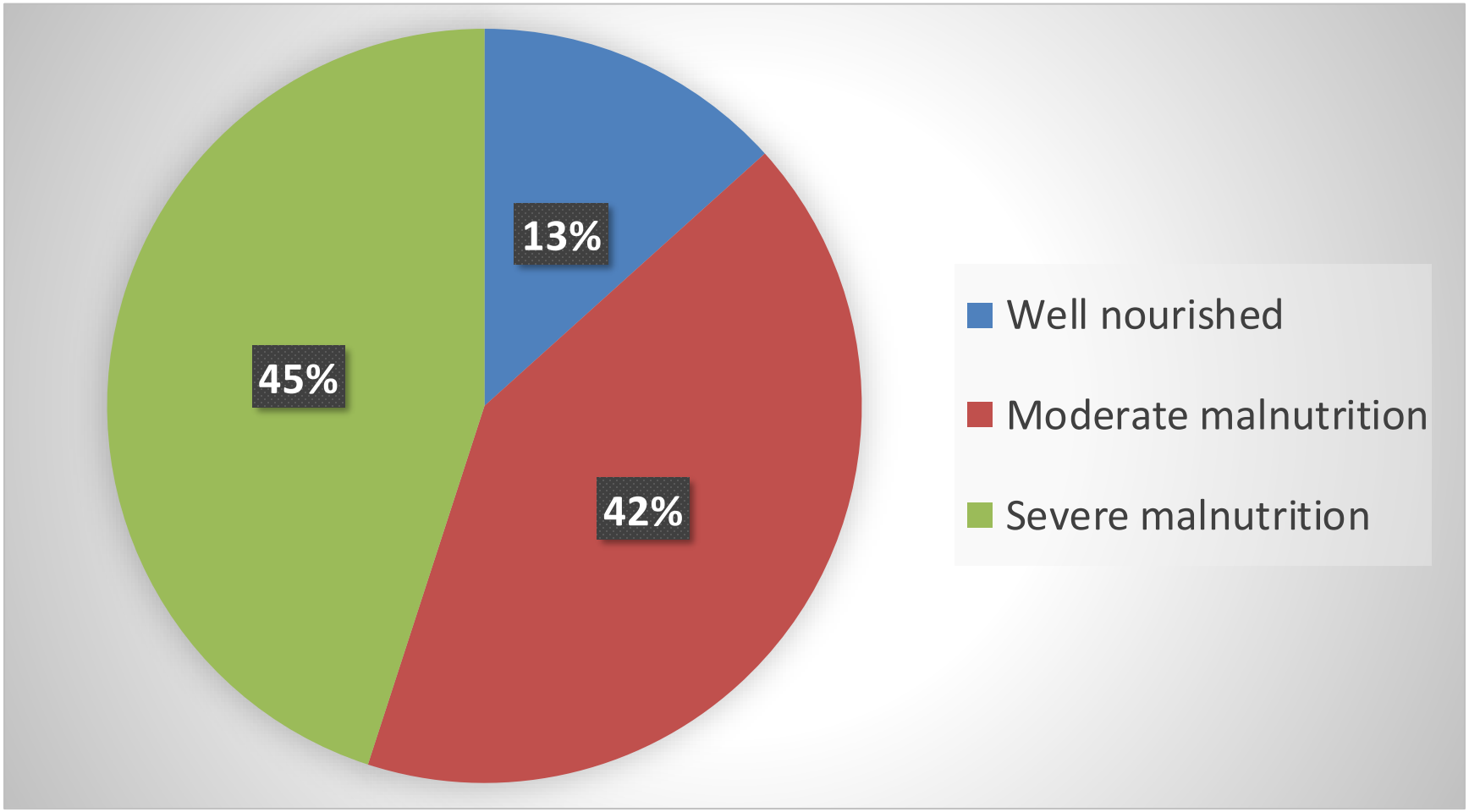


Figure 2: *The nutritional status of the children*

Baseline

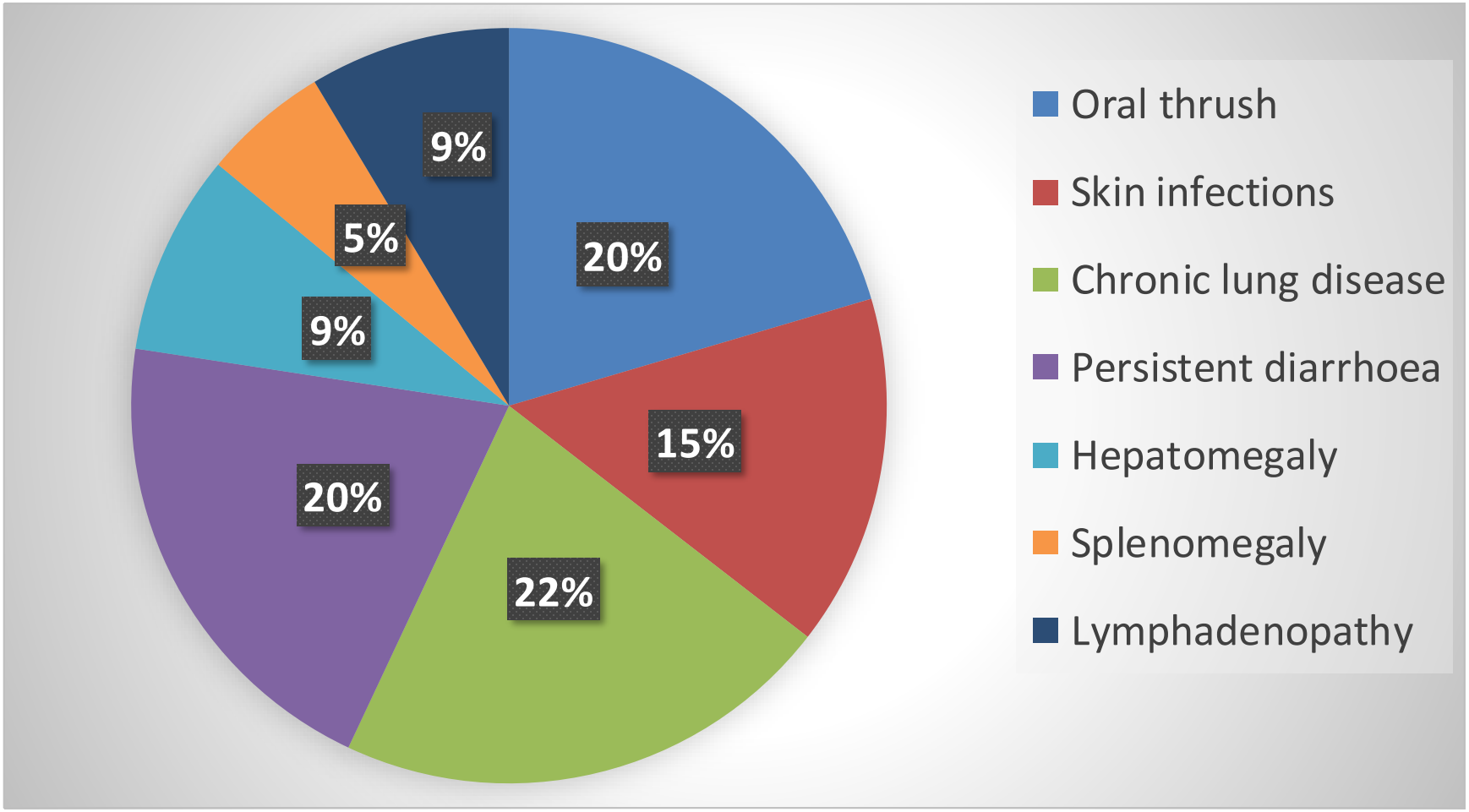
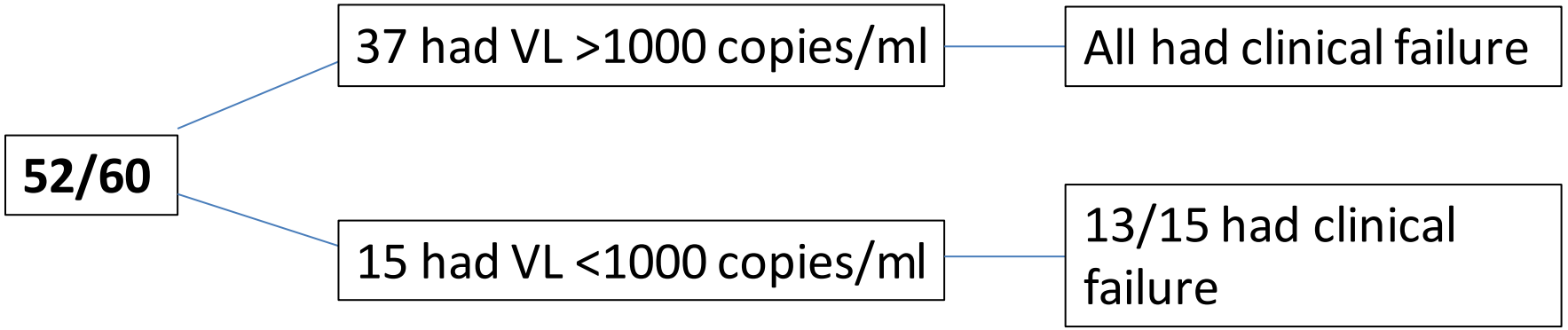


Figure 3: *Clinical features of immune deficiency (OI's) in the children*

Viral load test before switch in ART



- Median viral load was 12,163 copies/ml *(IQR 243-74,879)*
- Significant correlation between clinical and viral failure (Pearson chi2, p <0.001)

New ART regime

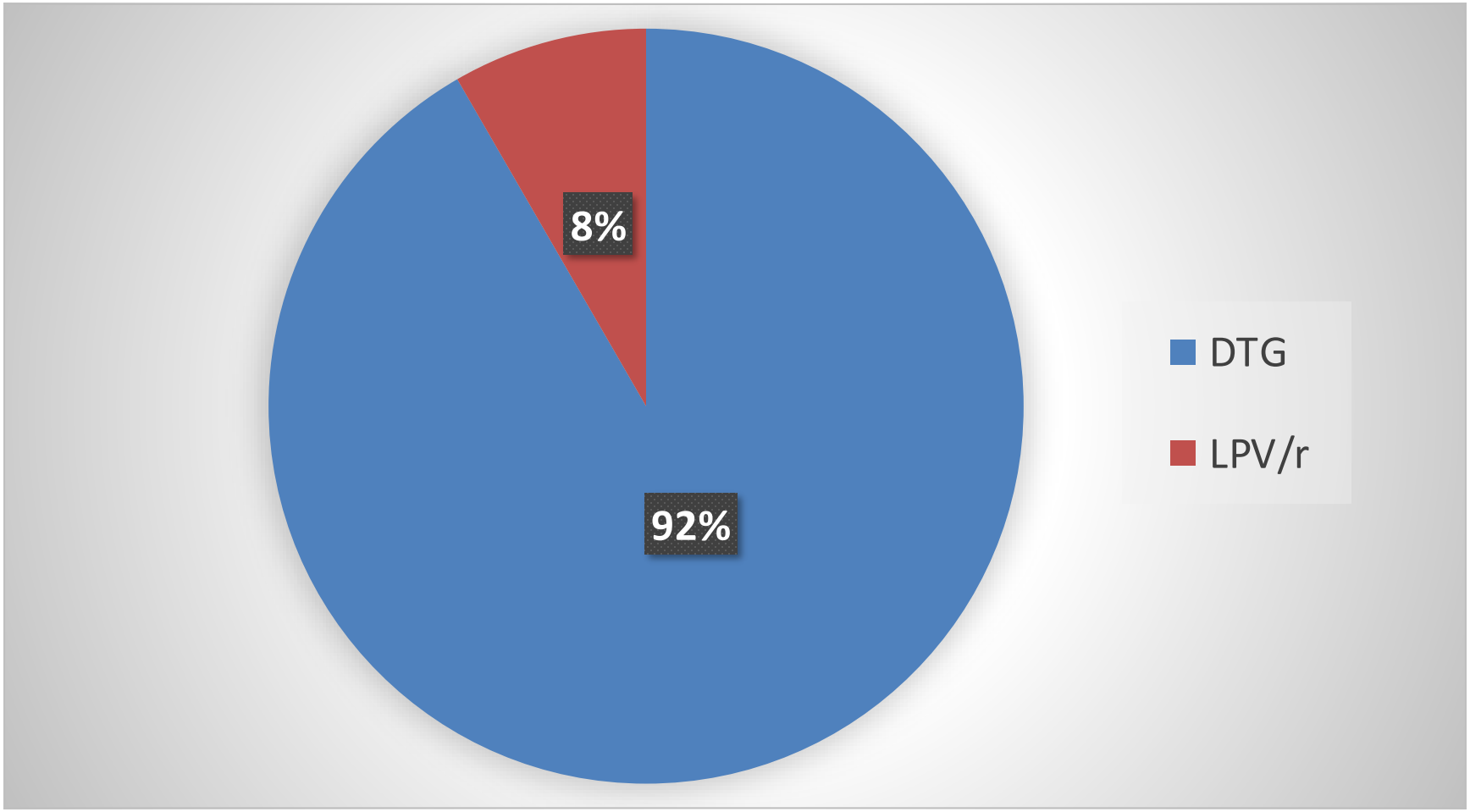
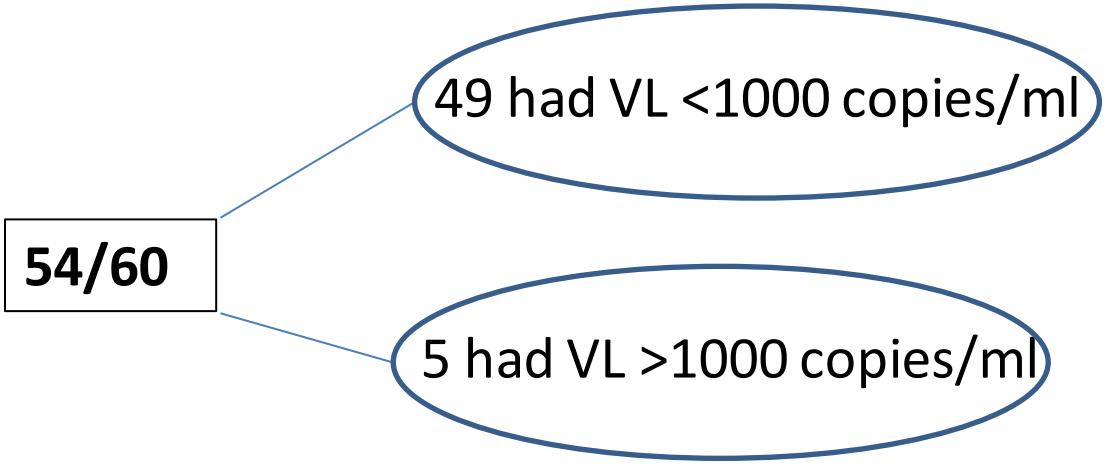


Figure 4: *The new ART regime the children are currently on*

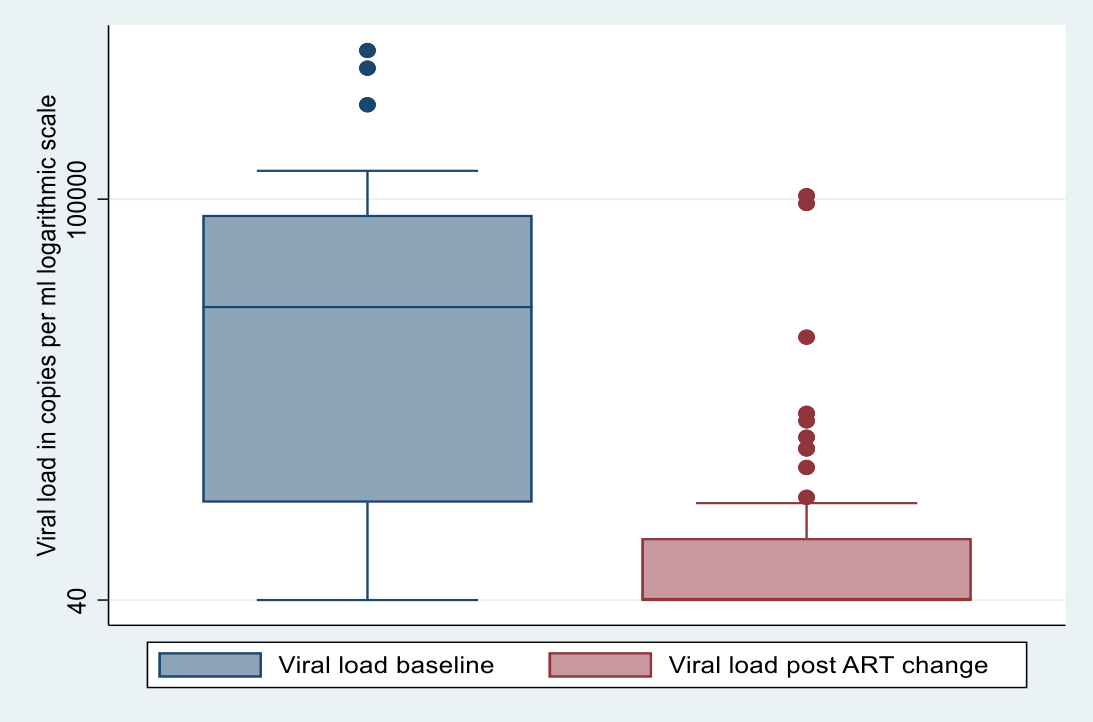
Viral load test after switch in ART



- *Median time of 19 months (IQR 11- 24 months)*
- *Median viral load of <40 copies/ml (IQR 0- 137 copies/ml)*

Significance of the VL test analysis

- **<u>Figure 5:</u>** *Viral load on baseline ART, and after change in ART to DTG or LPV/r based therapy*



Data not normally distributed *(paired t- test not ideal to use)* therefore the non-parametric (Wilcoxon sign- rank) test was used.

Discussion

- Prior to switch to DTG or LPV/r based therapy, many children living with HIV had severe virological and clinical failure, with opportunistic infections and severe malnutrition.

- In this study, 71% of children had virological failure and 75% had clinical failure with the old ART regimen.

- With the change to DTG based therapy, there was significant improvements in viral load, with 90% of having adequate viral suppression, and much improved clinical state.

Discussion

- A study done in Tanzania which included 200 children and adolescents (85.5% were treatment experienced with high adherence levels). 70.2% attained undetectable viral load 6 months after using the DTG based regimen ($p<0.05$).

- Randomized clinical trials across seven LMICs showed 80- 90% HIV RNA suppression rates 12 months after switch to the DTG and LPV/r based regimen.

- The change to DTG based therapy should be universal, and coupled with close monitoring of viral load and clinical and nutritional state.

Mutagonda. R. et. al published in June 2022

Vitoria M et.al March 2018

Limitations

- Observational nature of this study, which can be prone to bias because of some unmeasured confounders. This might have been reduced by:
  - *extending the duration and using other predictor parameters for follow ups on these children*

- No comparison or follow up regarding the effect of DTG on haematological parameters, renal and liver functions.

- Some samples for viral load testing were rejected at the laboratory due to sample insufficiency or incorrect labelling of specimen.

Conclusion

- DTG based therapies are the way forward as first- line ART regimen for children in PNG.

- We need ongoing monitoring of ART resistance; although DTG is less likely to develop resistance, it is inevitable overtime.

- It is important to extend the longitude of this study to monitor long term viral suppression and immune reconstitution, renal and liver function tests, clinical and nutritional outcomes, adherence and disease understanding for these children.

Acknowledgements

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