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**THE EFFECTIVENESS OF DOLUTEGRAVIR AMONG HIV POSITIVE  
ADOLESCENTS ATTENDING ART CLINIC AT BENUE STATE  
UNIVERSITY TEACHING HOSPITAL, MAKURDI, BENUE STATE, NIGERIA**

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### **Abstract**

**Background:** Globally, HIV is the second leading cause of death among adolescents. These adolescents (10-19 years) make up 8% of people living with HIV (PLWH) in Nigeria with an HIV prevalence rate of 1.4%. They have poorer adherence, retention and rate of viral suppression than HIV-infected adults. To curb these issues, Dolutegravir (DTG) which is the third HIV integrase inhibitor (INI) has been initiated for them and for most clients.

**Objective:** In other to measure the effectiveness of DTG, this study compared the treatment outcomes between other ART combination and DTG based regimen among HIV positive adolescents attending antiretroviral therapy (ART) Clinic in Benue State University Teaching Hospital (BSUTH) Makurdi, Benue state, Nigeria.

**Methods:** A comparative descriptive study was employed to review 27 HIV positive adolescents on DTG regimen over a four year period from the clients date of commencement of ARVs to December 2021 in BSUTH ART clinic. All the adolescents (27) who were regular at their clinic appointment within that period were included in the study. Those who were identified from records who had commenced ART prior to the study period and had been changed from previous ART combination to a DTG based regimen were analyzed. Outcome measures of interest were: (1) Virological response; (virological suppression when Target is not detected, viral load <50 which is low level viremia and viral load >50) (HIV-1 RNA viral load before and after commencement of DTG based ART regimen) (2) Intolerability (discontinuation) (3) Weight difference >1kg (at 0 and 6months of commencement of previous ART regimen without DTG and DTG based ART regimen)

**Results:** The mean age of respondents was approximately 14 years. Through period under review, virologic suppression rate was 82% (on-treatment analysis) for DTG based regimen and 11% for other ART based regimen. There were no discontinuations of DTG as it was well tolerated by the clients. By 6 months after commencement of DTG based regimen, the median change in weight for the study population was 9.1 kg on DTG regimen as compared to 3.5kg while on other ART based regimen.

**Conclusion:** In our cohort of adolescent male and female clients, DTG showed good virologic efficacy and was generally well tolerated.

**Recommendation:** More deliberate measures such as enhanced adherence counseling should be put in place to attain the 95-95-95 target among adolescent patients. Whether DTG results in undesirable weight gain or rather statistically significant results, remains a debate. Hence the use of DTG regimen for HIV-positive adolescents is strongly supported.

**Keywords:** Adolescents, Antiretroviral, Dolutegravir, Makurdi, Therapy.

## **Introduction**

Worldwide, about 2.1 million adolescents aged 10-19 years are living with HIV of which 160,000 are Nigerians. <sup>1</sup> National data also suggests that 40 percent of all reported new cases of HIV occur in young persons aged 15 to 24 which is the highest when compared to other age groups <sup>2</sup> However, the high-risk sexual behavior exhibited by adolescents results in their engagement in unprotected sex with multiple partners, transactional sex, being easily coerced into sex, and peer pressure. <sup>3</sup> Though analysis shows that the adolescent males engage in risky behavior than the females, <sup>3</sup> early sexual debut, marriage, and childbirth also makes female adolescents vulnerable to HIV infection. <sup>3,4</sup> High levels of stigma, gender inequality, punitive laws against repressed vulnerable groups, and poverty are identified structural factors that contribute and increase these vulnerabilities. <sup>3</sup> Compared to adult populations living with HIV, adolescents living with HIV (ALHIV) have a higher likelihood of suboptimal adherence, viral load progression, lost to follow-up, morbidity and mortality partly due to the aforementioned issues. <sup>5</sup> Additionally, toxicity, treatment failure, and resistance to existing HIV treatment regimens have become a challenge in resource-limited settings.

Whereas supporting evidence synthesis suggested favorable efficacy, tolerability and safety of dolutegravir (DTG) relative to EFV. <sup>6</sup> As a result, DTG which is the third HIV integrase inhibitor (INI) has been initiated for most clients <sup>7</sup> and in Nigeria, DTG fixed dose-based combination therapy was approved as the preferred first line ART in 2018.

However, a new side effect has been observed in recent years, associated with DTG in particular,

namely an unexpected excess in weight gain during the course of treatment. <sup>8</sup> The mechanism underlying weight gain and its' effect on the metabolic and cardiovascular outcomes is still unclear at this time. <sup>9</sup> Therefore; this study aimed to assess the virological effect and the side effects such as weight gain of DTG -based antiretroviral therapy among HIV positive adolescents attending ART clinic at Benue state university teaching hospital, Makurdi, Benue state, Nigeria .

## **Materials and methods**

### **Study Design**

This was a descriptive comparative study done by reviewing client record which was carried out starting from each clients' ART commencement on Efavirenz or Nevirapine based combination mostly from birth to 2018 when they were all changed to DTG and their progress up to December 2021.

### **Setting**

The ART Clinic of Benue State University Teaching Hospital (BSUTH) was used for the study. It is one of the clinics set up through funds obtained from the United States Presidential Emergency Plan for AIDS Relief (PEPFAR now APIN) program in Nigeria. Benue State University Teaching Hospital is a 300-bed State Government-owned Tertiary Healthcare Facility in Benue State, Nigeria. The ART clinic days are Tuesdays, Fridays every week (for adults and pediatric clients) and third Saturday of every month for adolescents with an average of 20 adolescents seen at each clinic. The clinic has a program for disclosure and all the adolescents used in this study have already been disclosed to.

### **Participants**

The study population was male and female adolescents aged 10 to 21 years (age range stipulated by the APIN program) on ART till date. The file

records of all the adolescents who had been changed from other regimen to DTG based regimen and were regular (did not miss attendance within the period of the study) at their hospital appointments and had good adherence were included in the study however those with incomplete file records were excluded.

### Sample size determination

Sample size was determined by using all the adolescents that attended the clinic because they were few in number (30) therefore, they were all included in the study. However those with incomplete records were excluded from the study (3 respondents).

### Data Sources/Management

The tools used were clients file records and a profoma based on the study objectives. The profoma captured clients' socio-demographic characteristics, weight at their ART commencement and 6 months

after (for both ART based regimen and DTG based regimen), significant weight gain or loss termed as weight gain >1kg or <1kg respectively, viral load records (virological suppression when Target is not detected, viral load <50 which is low level viremia and viral load >50) while on other ART regimen and one year after the change to DTG and any noted complaints of side effects or discontinuation of the DTG based regimen compared with other ART combination regimen. Data was analyzed using SPSS version 21.0. Categorical data are presented as frequencies and percentages. Statistical significance was set at P-value of 0.05.

### Ethical clearance

This was obtained from Benue State University Teaching Hospital (BSUTH) Health Research Ethics Committee (HREC)

## Results

**Table 1 showing socio-demographic characteristics, drug regimen and WHO staging of the respondents**

Variables	Frequency(N)	Percentage (%)
<b>Age(years)</b>		
<b>Mean 14 years</b>		
≤14years	19	70
15-17	5	19
18-21	3	11
<b>Sex</b>		
Male	12	44
Female	15	56
<b>Previous Regimen</b>		
AZT-3TC-NVP	17	63
AZT-3TC-EFV	2	7
TDF-3TC-EFV	3	11
ABC-3TC-LPV/r	5	19
<b>Current Regimen</b>		
TDF-3TC-DTG	19	70
ABC-3TC-DTG	8	30
<b>Side Effects of DTG based ART regimen</b>		
Weight gain	25	93
Weight loss	2	7
<b>Side of other ART regimen without DTG</b>		
Weight gain	20	74
Weight loss	2	7
No weight change	5	19
<b>WHO Staging</b>		
Stage I	19	70
Stage II	2	7
Stage III	5	19
Stage IV	1	4

**Abbreviations:** 3TC, Lamivudine; ABC, Abacavir; TDF, Tenofovir disoproxil fumarate. NVP, Nevirapine; EVZ, Efavirenz; LPV/r, Lopinavir/ritonavir;

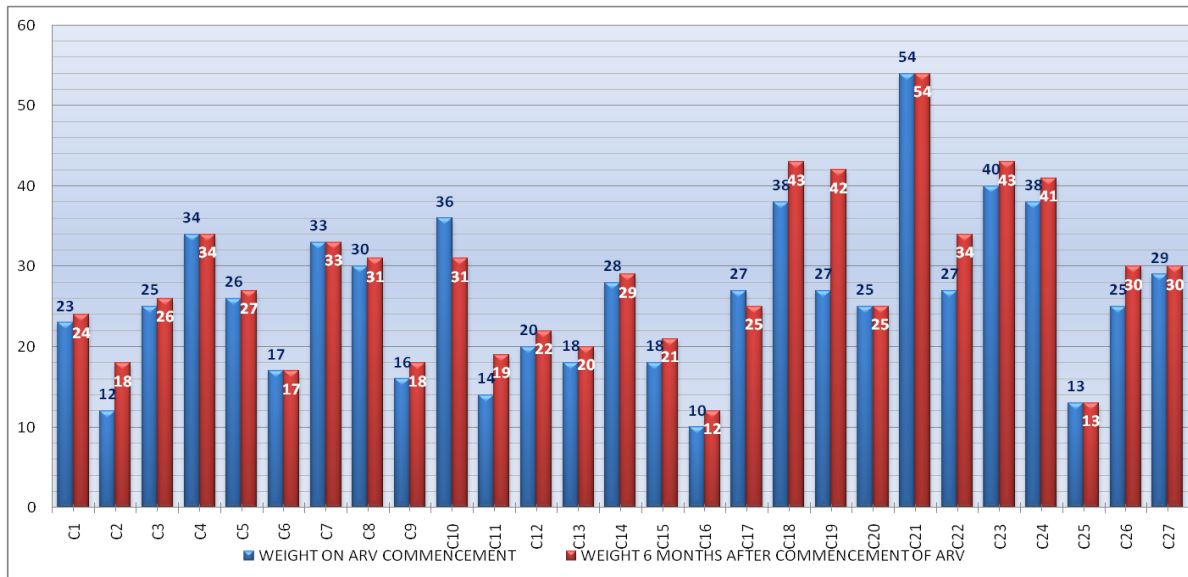
From table 1 above, 70% of the respondents are 14years and below, 56% are females. All the respondents (100%) were changed from their previous ART regimen to DTG based regimen, 93% of the respondents gained weight after the change to DTG regimen, no other side effects were observed among the respondents and 70% of the respondents presented at WHO stage I.

**Table 2 showing the viral load results of the respondents following ART regimen change**

Viral load categories Copies/ml	Viral load before change to DTG regimen N (%)	Viral load after change to DTG regimen N (%)	Fischer's (P-value)
TND	3 (11)	22 (82)	0.0001
<50	14 (52)	2 (7)	
≥50	10 (37)	3 (11)	
<b>Total</b>	<b>27(100)</b>	<b>27(100)</b>	

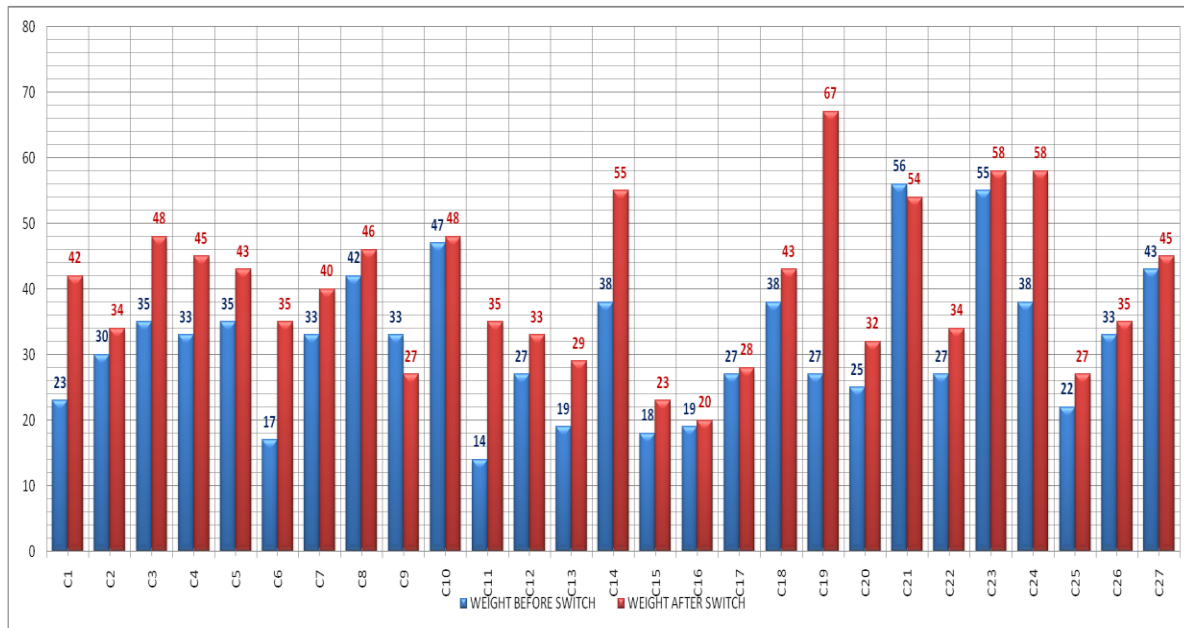
\*TND=Target not detected which is virological suppression, Viral load <50=Low level viremia; Viral load ≥ 50=Unsuppressed

Table 2 above shows that there is a statistically significant difference between the viral load before and after commencement of DTG based regimen commencement (p- 0.0001) with 82% of the respondents are virally suppressed.



\*Significant weight gain termed as weight gain >1kg

**Figure 1.** Chart showing the weight of respondents on commencement of ART without DTG and 6 months after , 74% of respondents gained weight whereas, 19% of them experienced no weight change and 7% had weight loss after commencement of ART. Average weight gain was 3.5kg



\*Significant weight gain termed as weight gain >1kg

**Figure 2.** Chart showing the weight of respondents before and after their change to DTG regimen and 93% of respondents gained weight 6 months after commencement of DTG regimen while 7% lost weight. Average weight gain was 9.1kg

### Discussion

Our study revealed that more female adolescents than males (table 1) are positive and active on regular clinic visits and ART at BSUTH which is in keeping with a report from the Global information and education on HIV and AIDS which showed that Young people (10 to 24 years) and adolescents (10 to 19 years), especially young women and young key populations, continue to be disproportionately affected by HIV.<sup>10</sup> Most of the adolescents in this study population are 14 years and below. This agrees with a study carried out in 2018, where 120 thousand adolescents and 140 thousand children in Nigeria had HIV. Per 1,000 uninfected population, the HIV incidence rate among children aged up to 14 years was 79%. Nigeria recorded in 2018 the highest rate

of children infected with HIV through their mothers worldwide.<sup>11</sup>

A comparative study conducted in university of Port Harcourt teaching hospital among children on the effect of DTG based regimen, revealed a statistically significant effect on suppressing viral load over a 6 months' period ( $X^2 = 53.77$ ,  $p = 0.0001$ )<sup>12</sup> which is similar with the findings of our study ( $p = 0.001$ ). The same study reported that 91.5% of respondents achieved a viral suppression at the end of 6 months also consistent with the findings of our study which showed that 82% of respondents had viral load suppression (TND).

Whereas the IMPAACT study showed that 70% of adolescents (12 to < 18 years old) treated with DTG achieve a complete viral suppression<sup>13</sup> which was below our findings. Despite these achievement with

DTG, the 95-95-95 target has not been attained probably due to poor adherence and risky sexual behavioral tendencies among adolescents.

Among our respondents while on NVP and EFV based combination for over 5years, only 11% had achieved complete viral suppression (TND) with 52% at the level of low level viremia (LLV). But when they were changed to DTG, they TND was achieved in 82% of the respondents. This is in line with a report from WHO indicated that viral load Suppression was found to be faster among those on DTG based regimens compared to EFV-based regimens. <sup>14</sup> It stated that 81% of patients who started with a DTG based regimen presented a suppressed viral load after 3 months of treatment, compared to 61% for those on an EFV-based regimen. <sup>14</sup>

The weight gain observed in our study showed that on commencement of other ART regimen, 74% of the respondents gained weight which was 3.5kg on the average as compared to when changed to DTG based regimen, 93% of them gained weight with an average of 9.1kg at 6 months. This may be attributed to the attendant viral suppression, less chances of Opportunistic infections and better living on changing to DTG. A similar finding was observed in a study where a total of 495 patients were included: 136 switched from EVF/TDF/FTC to an INSTI-containing regimen and 34 switched to a PI-containing regimen. Patients switched to an INSTI-containing regimen gained an average of 2.9 kg at 18 months compared to 0.9 kg among those continued on EFV/TDF/FTC (p=0.003) <sup>15</sup>

With regards to the side effects resulting in discontinuation of DTG regimen, non was reported among our clients compared to the other ARV based regimen with complaints of unpleasant taste of the drugs and frequency of the dosage. This is similar to

the findings in a study carried out among HIV-infected pediatric patients who experienced no adverse events were reported and most patients demonstrated a good adherence to treatment. <sup>16</sup> DTG was also statistically superior to EFV, EVG/c, ATV/r, LPV/r, and NVP with regards to rates of discontinuation due to adverse events (AEs) in another research. <sup>17</sup>

### **Conclusion**

In conclusion, the findings from this study indicates that adolescents will benefit from DTG- based regimen achieving a complete control of HIV infection with no side effects. The major advantages of DTG-based regimen are the prompt viral suppression, possibility to reduce the pill burden to two pills once a day, the increasing treatment adherence and the low or absent risk of additional drug resistance mutations. Whether DTG results in undesirable weight gain or rather statistically significant results, remains a debate and should be researched further.

### **Limitations**

Weight gain may be sign of improvement therefore further studies need to be conducted to compare specifically the weight gain using Body mass index on commencement of ART with Efavirenz and ART regimen with DTG among other health facilities.

### **Conflict of interest statement**

The authors declare that they have no competing interests.

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## References

1. Adolescents and Young People – UNICEF DATA. (2017). Available at: <https://data.unicef.org/topic/hivaids/adolescents-young-people/> Accessed 3<sup>rd</sup> of March 2022.
2. Idele, Priscilla, et al. “Epidemiology of HIV and AIDS among adolescents: current status, inequities, and data gaps.” JAIDS Journal of Acquired Immune Deficiency Syndromes 66 (2014): S144-S153.
3. National Population Commission- NPC/Nigeria and ICF International. Nigeria Demographic and Health survey 2013, Abuja, Nigeria: NPC/Nigeria and ICF International 2014. Available from: <https://dhsprogram.com>. Accessed on the 5<sup>th</sup> of March 2022
4. UNAIDS. 2017. Ending AIDS: Progress towards the 90-90-90 targets Available from: <https://www.avert.org/professionals/hiv-around-worlds/sub-saharan-africa/nigeria>. Accessed on the 18<sup>th</sup> of March 2022
5. Chhim K, Mburu G, Tuot S, et al. Factors associated with viral non-suppression among adolescents living with HIV in Cambodia: a cross-sectional study. AIDS Res Ther. 2018;15: 20. <https://doi.org/10.1186/s12981-018-0205-z>.
6. Kanters S, Vitoria M, Doherty M, et al. Comparative efficacy and safety of first-line antiretroviral therapy for the treatment of HIV infection: a systematic review and network meta-analysis. Lancet HIV;2016, 3 (11) e510–e20

7. Eden AM, Esileman AM, Kedir AG. Virological Suppression and Its Associated Factors of Dolutegravir Based Regimen in a Resource-Limited Setting: An Observational Retrospective Study in Ethiopia. HIV AIDS (Auckl) 2021;13:709-717.

8. Menard A, Meddeb L, Tissot-Dupont H, et al. Dolutegravir and weight gain: an unexpected bothering side effect? AIDS 2017; 31:1499–500. [Google Scholar](#)

[Crossref PubMed](#)

9. Bourgi K, Rebeiro PF, Turner M, et al. Greater weight gain in treatment-naive persons starting dolutegravir-based antiretroviral therapy. Clin Infect Dis 2020;70:1267–74. [Google Scholar](#)

10. Global information and education on HIV and AIDS. Accessed at <https://www.avert.org/professionals/hiv-social-issues/key-affected-populations/young-people> on the 10<sup>th</sup> of March

11. Health, Pharma & Medtech. Number of children and adolescents living with HIV in Nigeria in 2018, by age group. Accessed at <https://www.statista.com/statistics/1126655/children-and-adolescents-with-hiv-in-nigeria-by-age-group/> on the 10<sup>th</sup> of March 2022

12. Paul N. I&Ugwu R O. Dolutegravir (DTG) Based Fixed Dose Combination (FDC) of Tenofovir/Lamivudine/Dolutegravir (TLD) and Viral Load Suppression in Children in Port Harcourt, Nigeria, Journal of Scientific research and reports. 2020; 26(2):52- 59

13. PL MC. Dolutegravir: a review of its use in the management of HIV-1 infection in adolescents and adults. Drugs. 2014; 74:1241–52.

14. WHO (2018), Dolutegravir (DTG) and the fixed dose combination (FDC) of tenofovir/lamivudine/dolutegravir (TLD), Accessed at [https://www.who.int/hiv/pub/arv/DTG-TLD-arv\\_briefing\\_2018.pdf?ua=](https://www.who.int/hiv/pub/arv/DTG-TLD-arv_briefing_2018.pdf?ua=) on the 5<sup>th</sup> of March 2022

15. Jamison Norwood, Megan Turner, Carmen Bofill, Peter Rebeiro, Bryan Shepherd, Sally Bebawy et al. Weight Gain in Persons with HIV Switched from Efavirenz-based to Integrase Strand Transfer

Inhibitor-based Regimen. *J Acquir Immune Defic Syndr.* 2017; 76(5): 527–531.

16. Bruzzese, E., Lo Vecchio, A., Smarrazzo, A. et al. Dolutegravir-based anti-retroviral therapy is effective and safe in HIV–infected paediatric patients. *Ital J Pediatr.* 2018; **44**, 37.  
<https://doi.org/10.1186/s13052-018-0469-x>

17. Kanters S, Vitoria M, Doherty M, Socias ME, Ford N, Forrest JI, et al. Comparative efficacy and safety of first-line antiretroviral therapy for the treatment of HIV infection: a systematic review and network meta-analysis. *Lancet HIV.* 2016;3(11):e510–e20.