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Research Article

The Clinical Efficacy of Integrating Dolutegravir into the Conventional Therapeutic Regimen for HIV Management

Nikita Doke, Simran Hajgude, Avinash Dhande, Shobha Tole*, Shivshankar Gunjegaonkar, Amol Joshi

ASPM's K. T. Patil College of Pharmacy, Dharashiv, Maharashtra, India.

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ABSTRACT

This study investigates the efficacy of transitioning from Tenofovir/Lamivudine/Efavirenz (TLE) to Tenofovir/ Lamivudine/ Dolutegravir (TLD) as a first-line antiretroviral therapy for the management of HIV. A retrospective analysis was conducted involving 261 individuals in whom 145 patients were initially treated with TLE in 2017 who were transitioned to TLD in 2020 and 116 patients were given TLD as first-line therapy from 2020 onwards. Clinical parameters like viral load (VL), CD4 cell count, and WHO clinical stage were evaluated at baseline to study the effectiveness of the treatment. In addition, the non-clinical variables like age, sex, weight, mode of transmission and body mass index (BMI) were analyzed. The results signified enhancements in CD4 count, viral load and weight across both groups (TLE to TLD transition and TLD initiated as first-line therapy) with a statistical significance of $p < 0.001$***. The median BMI for patients transitioning from TLE to TLD was 21.63 (IQR 19.62-24.37) with a *p-value* of 0.004**, while the median BMI for patients on TLD as a first-line therapy was 20.83 (IQR 18.95-23.87), exhibiting a *p-value* of 0.115ns indicating no substantial difference between both groups. The findings showed effective viral suppression, with viral loads categorized as target not detected (TND) and CD4 counts exceeding 500 cells/mm^3. Overall, the integration of TLD into the ART regimen resulted in improved clinical outcomes and sustained viral suppression among the patients showing the advantage of this therapeutic transition in HIV management.

Introduction

Human ımmunodeficiency virus (HIV) infection is still a significant global health problem, characterized by its ability to progressively weaken the body's immune system, which leads to acquired immunodeficiency syndrome (AIDS) if left untreated. The introduction of antiretroviral therapy (ART) has transformed HIV infection from a fatal disease to a manageable chronic condition, significantly enhancing life expectancy and improving the quality of life for affected individuals.[1] In the global epidemiological context, HIV infection has been associated with approximately 40.1 million fatalities to date. By the end of 2022, an estimated 39 million individuals were living with HIV worldwide, with the majority (approximately 25.6 million) located in the African region. In 2022 alone, an estimated 630,000 deaths resulted from HIV-related causes, while approximately 1.3 million new HIV infections occurred.[2] These statistics underscore the ongoing impact of HIV/AIDS on a global scale, highlighting the continued need for effective prevention, diagnosis, and treatment efforts. In India, HIV/AIDS remains a significant public health concern, with an estimated 2.3 million people living with HIV in 2022.

Although the prevalence of HIV in India has declined in recent years, certain regions and populations remain disproportionately affected by the epidemic. Key populations at higher risk of HIV infection in India include men who have sex with men, transgender individuals, female sex workers, and people who inject drugs. Efforts to combat HIV/AIDS in India have included widespread testing

***Corresponding Author:** Dr. Shobha Tole

Address: ASPM's K. T. Patil College of Pharmacy, Dharashiv, Maharashtra, India.

Email ✉**:** shobhatole@gmail.com

Tel.: +91-9421710605

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and counseling services, the provision of antiretroviral treatment, and targeted prevention interventions tailored to high-risk populations.[3] Despite the remarkable progress made in HIV treatment, challenges persist in achieving optimal outcomes for all patients. Traditional ART regimens typically comprised combinations of nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (INSTIs). While these regimens have been effective in suppressing viral replication and reducing HIV-related morbidity and mortality, treatment failure and drug resistance remain significant concerns.[4] Treatment failure often occurs due to various factors, including poor treatment adherence, drug toxicity, and the development of drug-resistant viral strains.[5] Additionally, the complexity and pill burden associated with older ART regimens has been associated with challenges in maintaining adherence and achieving sustained viral suppression.

In October 2020, a significant shift occurred in HIV treatment protocols with the introduction of dolutegravir (DTG) as a first-line therapy (FLT), replacing efavirenz (EFZ) as recommended by the World Health Organization (WHO).[6] The primary rationale behind this transition was the inadequacy of EFZ in achieving therapeutic outcomes such as viral suppression, genetic barrier of drug resistance, and drug-drug interactions. Numerous studies have highlighted the superior efficacy, simplified administration procedures, and reduced occurrence of adverse effects associated with DTG compared to EFZ and other available medications.[7-9] Before the introduction of DTG, HIV-positive individuals were commonly treated with triple combination therapy, known as TLE, which included EFZ. However, this regimen often failed to reduce viral load (VL) or raise CD4 count adequately. The decision to switch to a TLD regimen containing dolutegravir was supported by newly assessed data appraising benefits and risks.[10] The WHO advocated for the adoption of DTG as both first- and second-line therapy for all demographic groups in the treatment of HIV infection, recognizing its potential to improve treatment outcomes and mitigate the emergence of drug resistance.[11] In comparison to the earlier therapy containing efavirenz, dolutegravir offers a compelling alternative with superior efficacy, reduced toxicity, and a higher genetic barrier to resistance.[12] The evidence supporting this transition underscores the importance of optimizing HIV treatment regimens to achieve maximal therapeutic benefits while minimizing the risk of treatment failure and drug resistance.

Through the integration of dolutegravir into conventional therapeutic protocols, healthcare providers can further enhance the management of HIV infection and improve the long-term prognosis for affected individuals.[7,13] The clinical indications for incorporating dolutegravir into HIV treatment protocols are multifaceted. Dolutegravir-based regimens are recommended as first-line therapy for treatment-naive individuals owing to their potent antiviral activity, favorable tolerability, and reduced risk of virological failure.[14] Furthermore, dolutegravir is recommended for use in treatment-experienced patients with viral resistance to older antiretroviral agents, offering a viable salvage therapy option for individuals with limited treatment options.[15]

In this study, we aim to assess the clinical effectiveness of integrating dolutegravir into conventional therapeutic regimens for managing HIV. We will investigate its impact on critical aspects such as viral suppression, immune system restoration, treatment adherence, and overall antiretroviral therapy for patient well-being. Our analysis seeks to uncover the potential advantages and challenges associated with dolutegravir-based antiretroviral therapy through an exhaustive review of existing literature and clinical data. Despite the lack of specific clinical outcomes regarding the DTG regimen and a systematic comparison between TLE and TLD from 2017 to 2022 at the Civil District Hospital, our study closely evaluates 261 patients for clinical outcomes and their transition to the triple regimen. By shedding light on these findings, we aim to offer valuable insights that can shape clinical practices and drive future research endeavors in the dynamic field of HIV/AIDS management.

Materials and Methods

Study Design and Setting

The data for this study were gathered meticulously by reviewing medical records and patient profile forms from the ART department of Civil District Hospital Dharashiv, Maharashtra, India. Additionally, computerized data from the hospital's database were used to ensure accuracy and comprehensiveness. This approach minimized the risk of bias and provided a thorough understanding of each patient's medical history and treatment progress.

The study focused on individuals living with HIV and analyzed data from six years. Its goal was to assess the clinical effects of introducing DTG into the standard HIV treatment regimen. In the public healthcare clinics of the district civil hospital, ART delivery involved regular clinical assessments, including viral load testing, CD4 count monitoring, and assessing the WHO clinical stage. Viral load tests were conducted six and twelve months after starting ART and annually after that. CD4 count measurements were taken at the beginning of ART and twelve months later, with additional tests as needed based on clinical indicators. Patients who experienced virological failure, defined as two consecutive viral loads of 1000 copies/mL or higher, were advised to switch to a second-line ART regimen containing NNRTIs like efavirenz or nevirapine.[16] Notably, routine HIV drug resistance testing was not performed when first-line ART failed in this setting.

The study aimed to provide insights into the real-world effectiveness of incorporating DTG into HIV treatment at the specified healthcare facility. This information would help inform decision-making and improve patient care. The study spanned twelve months, from June 2022 to June 2023, which was considered sufficient to gather a representative sample of patients receiving both traditional and new antiretroviral treatments and analyze their clinical outcomes over this period.

Study Population

The study included patients diagnosed with HIV, aged one year or older, from 2017 to 2023. It focused on two groups: those receiving the old treatment regimen (TLE+TLD) and those starting directly on the new regimen (TLD) with DTG. Patients with other health conditions or who were pregnant were excluded to keep the study group consistent. In total, 261 patients were involved: 145 received both old and new regimens between 2017 and 2023, and 116 started the new regimen with DTG along with tenofovir and lamivudine from 2020 onwards. The study aimed to explore the effects of adding DTG to standard HIV treatment in patients who switched to second-line ART within the specified timeframe. Ethical approval was obtained from the Institutional Ethical Committee.

Clinical and Non-clinical Assessment

We expressed the clinical assessment data for CD4, viral load (VL), BMI, weight, and WHO clinical stage change as median and interquartile ranges (IQR) to understand both the center and spread of the data. The non-clinical parameters like age, gender, and mode of transmission (MOD)[17,18] were considered for assessment. The CD4 count is considered as ≥ 500 cells/mm^3, while the viral load (VL) count is ≤ 300 copies/mL.[15,24] BMI was categorized as underweight (< 18.5 kg/m^2), normal (≥18.5–< 25.5 kg/m^2), overweight (≥25.5–< 30.5kg/m^2) and obese (≥ 30.5 kg/m^2).[19,20] MOD was categorized as Heterosexual, Mother-to-child, men having sex with men (MSM), blood transfusion, and unknown. Overall age was calculated as a median to represent the central tendency and then expressed as numbers and percentages, categorized as <18, 18–64, and ≥65 years.[14]

WHO Clinical Stages Assessment

Patients were categorized into one of the four cumulative clinical stages under the WHO classification from stage I (asymptomatic) to stage IV (AIDS). When a patient meets the requirements for a certain stage, at least one of the stages' clinical conditions is assigned to them.[9,21] Patients in stage I are asymptomatic and have chronic lymphadenopathy.[22] Clinical stage II is referred to as the mild asymptomatic stage with less than 10% of the total body weight and repeated respiratory diseases such as bronchitis and pharyngitis, along with some dermatological conditions, such as oral ulcerations, fungal and nail infection, seborrhea dermatitis. The moderately symptomatic stage is considered as WHO clinical stage III with more than 1 month of persisting symptoms like pulmonary tuberculosis, diarrhea, and chronic bacterial infections (pneumonia, meningitis, bone and joint infections, and bacteremia). The severely symptomatic stage like AIDS, named WHO clinical stage IV, CNS toxoplasmosis, HIV encephalopathy, extrapulmonary TB, pneumocystis pneumonia, chronic (more than 1 month) or orolabial herpes simplex infection, Kaposi's sarcoma and esophageal candidiasis are also associated with the clinical stage IV.[22,23] Changes in the WHO clinical stage from patients' initial phase (before receiving TLD as first-line treatment) to their final phase (after receiving TLD as FLT).

Statistical Analysis and Data Assessment

Data from medical records, patient forms, and computerized records were organized into a standard format for analysis. We used the paired t-test to compare pre and post-treatment clinical outcomes in patients receiving both TLE and TLD regimens. This statistical test was chosen because it's suitable for analyzing changes in clinical outcomes and data distribution. For categorical variables, we created a frequency table (Table 1), expressing values as numbers, percentages, median, and interquartile ranges. Continuous variables (Table 2), such as CD4 and viral load changes over time, were expressed as median ± standard deviation (SD). A significance level of $p \leq 0.05$ was set for statistical significance, denoted by asterisks (*). We used one asterisk for $p < 0.05$, two (**) for $p < 0.01$, and three (***) for $p < 0.001$. This threshold was chosen to minimize type I errors and ensure the reliability of the study findings. Data analysis was conducted using Microsoft Excel and GraphPad Prism (Version 10.1.1).

Results

Patients Baseline Characteristics

The comprehensive analysis of 261 HIV-infected patients provided significant insights into various aspects of the condition, shedding light on demographic patterns, modes of transmission, and treatment efficacy within the studied population. Regarding demographics, the gender distribution revealed a relatively equal representation of females 132 (50.57%) and males 129 (49.43%), indicating a diverse sample. The median age of 40 years, with an inter quartile range (IQR) of 31 to 48 years, suggested that the majority of patients fell within the prime adult age group of 18 to 64 years (n = 244). This broad age distribution underscores the prevalence of HIV across different age brackets and emphasizes the importance of tailored interventions for individuals of varying ages.

Mode of Transmission

Heterosexual transmission (n = 236) emerged as the predominant route, with the majority of cases attributed to this mode. This highlights the significance of targeted prevention efforts aimed at individuals engaged in heterosexual activities. Additionally, while less common, instances of mother-to-child transmission (n = 16), MSM (n = 4), and blood transfusion (n = 1) were also observed, indicating the diverse pathways through which HIV can be transmitted. These findings underscore the need for multifaceted prevention strategies that address the specific needs of various risk groups.

Dıfferences of TLE to TLD Regimen in Concern to BMI, CD4 and Viral Load Count

Patients on the TLD regimen exhibited a higher median BMI of 20.83 (IQR 18.95–23.87) compared to those on the TLE regimen, whose median BMI was 19.53 (IQR 17.22–22.26). Moreover, transitioning to the TLD regimen was associated with a significant increase in median CD4 count from 367 (IQR 229–490) to 479.5 (IQR 374.25–658.5). This shift indicated enhanced immune function and HIV management efficacy.

Additionally, the study observed a median viral load count of 57999 (IQR 7334–238030.5) during the TLE regimen, suggesting active viral replication. However, this viral load count may have been influenced by various factors such as treatment adherence and duration. These findings underscore the importance of evolving treatment strategies that not only improve individual health outcomes but also contribute to broader public health goals, such as reducing the spread of HIV within communities.

Clinical Significance for the Transition from TLE to TLE + TLD

The transition from a regimen comprising treatment experienced (TLE) to one incorporating both treatment naïve (TLD) and TLE (TLE+TLD) demonstrated significant clinical implications, as revealed by key clinical parameters observed in the study.

Firstly, the median CD4 count among patients receiving TLE+TLD was markedly higher compared to those solely on TLE, with a median of 591 (IQR 462–780) versus 367 (IQR 229–490), respectively. This difference was statistically significant (p <0.001***), indicating a substantial improvement in immune function following the transition to the combined regimen. A higher CD4 count is crucial in HIV management as it signifies better immune system health and reduces the risk of opportunistic infections. Secondly, the viral load (VL) in patients on TLE+TLD was consistently undetectable (TND), which was statistically significant at p <0.001***. Achieving an undetectable viral load is a key goal in HIV treatment, as it not only indicates effective suppression of the virus but also greatly reduces the risk of HIV transmission to others.

Table 1: Clinical and non-clinical baseline characteristics of HIV patients at ART, 2017-2022 (n = 261)

	TLE	*TLD*	*Total (261)*
Gender			
Female	84 (57.93%)	48 (41.37%)	132 (50.57%)
Male	61 (47.06%)	68 (58.62%)	129 (49.42%)
Age (median)	38 (30–47)	40 (35–48)	40 (31–48)
<18	10 (6.89%)	2 (1.72%)	12 (4.59%)
18-64	132 (91.03%)	112 (96.55%)	244 (93.48%)
>=65	3 (2.06%)	2 (1.72%)	5 (1.91%)
Mode of transmission			
Heterosexual	129 (88.96%)	107 (92.24%)	236 (90.42%)
Mother-to-child	12 (8.27%)	4 (3.44%)	16 (6.13%)
MSM	1 (0.68%)	3 (2.58%)	4 (1.53%)
Blood transfusion	0 (0%)	1 (0.86%)	1 (0.38%)
Unknown	3 (2.06%))	1 (0.86%)	4 (1.53%)
CD4 count median (IQR)	367 (229–490)	479.5 (374.25–658.5)	560 (412–720)
VL median (IQR)	57966 (7334-238030.5)	TND	TND
BMI median (IQR)	19.53 (17.22–22.26)	20.83 (18.95–23.87)	21.30 (19.46–24.22)

N- numbers; TLE- Tenofovir/Lamivudine/efavirenz; TLD- Tenofovir/Lamivudine/Dolutegravir; MSM- Men who have sex with men; CD4- Clusters of differentiation; VL- Viral load; IQR- Interquartile range; TND- Target Not Detected; BMI- Body mass index

This finding underscores the potent antiviral efficacy of the combined TLD and TLE regimen in controlling HIV replication. Furthermore, the transition from TLE to TLE+TLD demonstrated statistical significance (p = 0.004**) concerning body mass index (BMI). Patients transitioning to the combined regimen exhibited a notable increase in median BMI from 19.53 (IQR 17.22–22.26) to 21.63 (IQR 19.62–24.37). This suggests potential improvements in metabolic health or body composition following the transition, which is significant for overall health and well-being in HIV-positive individuals. Additionally, the study elucidated significant weight alterations in patients transitioning from TLE to TLE+TLD, with a median shift from 48 (IQR 40–55) to 53 (IQR 45–68). This weight gain was statistically significant (p < 0.001***), indicating potential positive effects on nutritional status and overall health in patients receiving the combined regimen.

Overall, these findings underscore the clinical efficacy and impact of transitioning to a combined TLD and TLE regimen in HIV-positive individuals. The observed improvements in immunological and virological outcomes, as well as weight management, highlight the importance of optimizing treatment strategies to enhance overall health and quality of life for patients living with HIV.

The Clinical Importance of TLD Therapy to Control HIV Infection

Table 2 provides further insight into the clinical outcomes among a subset of 116 patients who initiated direct TLD therapy as a first-line intervention (FLI) within the larger cohort of 261 patients. This subset's clinical parameters, including CD4 counts, viral load (VL) status, and weight, were closely examined before and after the initiation of TLD treatment, revealing significant improvements across multiple domains. At the time of diagnosis, the median CD4 count among these 116 patients was 340 (IQR 234.2–421.2). Following the commencement of TLD treatment, there was a remarkable increase in the median CD4 count to 479.5 (IQR 374.2–685.5). This elevation was statistically significant (p < 0.001***), underscoring the potent immunological benefits associated with TLD therapy.

Such a substantial rise in CD4 count reflects enhanced immune function, which is crucial for combating HIV-associated complications and improving overall health outcomes. Moreover, within this subset of patients receiving TLD therapy, viral load suppression was uniformly achieved, with all cases exhibiting undetectable VL, Target not detected (TND).

This outcome holds significant clinical importance as it signifies effective control of HIV replication and greatly reduces the risk of disease progression and transmission. The statistical significance of this result (p <0.001***) reinforces the robust antiviral efficacy of TLD therapy in achieving virological suppression among HIV-positive individuals.

The Transition from Diagnosis to after TLD

Additionally, notable weight gain was observed in these patients following the initiation of TLD treatment. The median weight increased from 50 (IQR 43–56.2) at the time of diagnosis to 53 (IQR 46–60) post-TLD treatment initiation. This weight gain was highly significant (p <0.001***), indicating favorable outcomes in weight management associated with TLD therapy. Improved nutritional status and weight management are essential components of HIV care, contributing to overall health and well-being.

In summary, the findings from this subset analysis underscore the comprehensive clinical benefits of direct TLD therapy as a first-line intervention in HIV-positive individuals. These benefits include significant improvements in immunological parameters, achievement of virological suppression, and promotion of favorable weight management outcomes. Such outcomes highlight the efficacy of TLD therapy in enhancing overall health and quality of life for individuals living with HIV.

WHO Clinical Stage Changes

The data from Table 3 offers valuable insights into the changes in WHO clinical stages among patients receiving different treatment regimens, specifically comparing those on TLE+TLD (n = 145) and TLD alone (n = 116). The analysis reveals notable patterns in clinical stage transitions, shedding light on the stability and progression observed within each treatment group.

Among patients receiving TLE+TLD, the majority (54.48%, n = 79) remained in stage I throughout the observation period, indicating a consistent level of stability in their clinical status. A smaller proportion of patients transitioned from stage II to I (24.82%, n = 36), suggesting an improvement in their clinical condition. Furthermore, an even smaller percentage moved from stage III to I (2.75%, n = 4), indicating a significant positive shift in disease severity towards a less advanced stage. Conversely, among patients on TLD alone, 48.27% (n = 56) remained in stage I, demonstrating a similar level of stability compared to the TLE+TLD group.

However, noteworthy transitions between different stages were observed within this group. Specifically, 20.68% (n = 24) of patients transitioned from stage II to I, indicating an improvement in clinical status similar to the TLE+TLD group. Additionally, 6.03% (n = 7) of patients moved from stage III to I, signifying a substantial positive shift towards a less severe disease stage. These findings underscore the predominance of stability in stage I among patients receiving TLE + TLD, suggesting the effectiveness of this combined regimen in maintaining or improving clinical status. Additionally, the transitions observed between stages I, II, and III among patients with TLD alone highlight

Table 2: Clinical significance and outcomes from TLE to TLE+TLD treatment

	The transition from TLE to TLE+TLD			*The transition from diagnosis to after TLD*		
	TLE	*TLE+TLD*	*p-value*	*Diagnosis*	*TLD*	*p-value*
	(n = 145)			*(n = 116)*		
CD4 (median)	367 (229–490)	591 (462–780)	<.001***	340 (234.2–421.2)	479.5 (374.2–658.5)	<.001***
VL (median)	57966 (7334-238030)	TND	<.001***	6603.5 (3956.5-48314.3)	TND	<.001***
BMI (median)	19.53 (17.22–22.26)	21.63 (19.62–24.37)	0.004**	19.39 (17.29–22.48)	20.83 (19-23.87)	0.115^{ns}
<18.5	58 (13.7)	20 (40)	0.619^{ns}	48 (41.3)	25 (21.5)	0.369^{ns}
18.5–25.5	78 (66.5)	98 (53.7)	0.634^{ns}	56 (48.2)	76 (65.5)	0.120^{ns}
25.5–30.5	5 (12.41)	18 (3.4)	0.197^{ns}	11 (9.4)	14 (12.0)	0.950^{ns}
≥30.5	4 (6.2)	9 (2.7)	0.250^{ns}	1 (0.8)	1 (0.8)	-
Weight (median)	48 (40–55)	53 (45–68)	<.001***	50 (43–56.2)	53 (46–60)	<.001***

N- numbers; TLE- Tenofovir/Lamivudine/efavirenz; TLD- Tenofovir/Lamivudine/Dolutegravir; CD4- Clusters of differentiation; VL- Viral load; IQR- Interquartile range; TND- Target Not Detected; BMI- Body mass index; The values with asterisks (*) represents the highly statistical significance *p-value*, ns- non-significant.

Table 3: WHO clinical stage change transition from Initial stage to the final stage.

Stage		*TLE+TLD (n=145)*		*TLD (n=116)*	
Initial	*Final*	*N*	*%*	*n*	*%*
I	I	79	54.48	56	48.27
	II	8	5.51	7	6.034
	III	2	1.37	1	0.86
	IV	0	0	0	0
II	I	36	24.8	24	20.69
	II	4	2.75	12	10.34
	III	0	0	4	3.44
	IV	0	0	0	0
III	I	4	2.75	7	6.03
	II	7	4.82	5	4.31
	III	2	1.38	0	0
	IV	0	0	0	0
IV	I	1	0.69	0	0
	II	2	1.38	0	0
	III	0	0	0	0
	IV	0	0	0	0

n- Number; TLE- Tenofovir/Lamivudine/Efavirenz, TLD-Tenofovir/Lamivudine/Dolutegravir; I- clinical stage I; II- Clinical stage II; III- Clinical stage III; IV- clinical stage IV.

the dynamic nature of HIV disease progression and the potential for favorable clinical outcomes with appropriate treatment interventions.

Overall, this analysis provides valuable insights into the impact of different treatment regimens on the clinical progression of HIV infection, guiding clinicians in optimizing treatment strategies to achieve favorable outcomes for patients.

Clinical Significance of TLE+TLD to TLD on CD4 Count

The comparison of CD4 count between patients initially treated with TLE+TLD and those on TLD alone reveals important clinical insights into the efficacy of these treatment regimens in managing HIV infection and bolstering immune function.

Among the 145 patients initially treated with TLE+TLD, the mean CD4 count showed a notable increase over time. In 2017, the mean CD4 count was 489.20 ± 434.09 cells/mm^3, which increased to 333.75 ± 202.79 cells/mm^3 in 2020 and further improved to 373 ± 164 cells/mm^3 by 2022. This upward trend in CD4 count indicates a positive response to treatment, with patients experiencing gradual improvements in immune function over the observation period. In comparison, among the 116 patients treated with TLD alone, a similar trend of increasing CD4 count was observed. In 2017, the mean CD4 count was 651 ± 287 cells/mm^3, which decreased slightly to 481 ± 166 cells/mm^3 in 2020 before rising again to 572.42 ± 181.65 cells/mm^3 by 2022. Despite the initial higher CD4 count in patients on TLD alone, the subsequent fluctuations followed a similar pattern to those observed in the TLE+TLD group, with overall improvements noted by 2022. These results underscore the significant increase in CD4 count observed in both treatment groups over time, highlighting the effectiveness of TLE+TLD and TLD alone in boosting immune function among HIV-positive individuals. The findings suggest that both treatment regimens contribute to the restoration and maintenance of immune health, thereby reducing the risk of opportunistic infections and enhancing overall well-being in patients living with HIV.

Overall, the data advocate for the clinical significance of TLE+TLD and TLD alone in promoting favorable

outcomes in CD4 count, indicating the importance of early initiation and adherence to antiretroviral therapy in the management of HIV infection.

Clinical Significance of TLE+TLD to TLD on VL

The comparison of viral load (VL) between patients initially treated with TLE+TLD and those on TLD alone provides crucial clinical insights into the effectiveness of these treatment regimens in suppressing HIV replication and managing disease progression.

Among the 145 patients initially treated with TLE+TLD, the mean VL exhibited fluctuations over the observation period. In 2017, the mean VL was 15328 ± 253085 copies/mL, which slightly increased to 17181 ± 48449 copies/mL in 2020 before rising further to 71690 ± 177833 copies/mL by 2022. Despite the fluctuations, the overall trend indicates a notable decrease in VL from 2017 to 2020, followed by a subsequent increase by 2022, albeit remaining at lower levels compared to the initial values.

In comparison, among the 116 patients treated with TLD alone, a consistent decrease in mean VL was observed over time. In 2017, the mean VL was 13528.46 ± 5263.53 copies/mL, which decreased to 4993.52±3309.31 copies/mL in 2018, further declining to 4446.50 ± 2711.50 copies/mL in 2019, and dropping significantly to 217.62 ± 780.91 copies/mL by 2020. However, there was a notable increase in mean VL in 2021 (33663.67 ± 18082.50 copies/mL) before decreasing again to 1306 ± 711 copies/mL by 2022.

These findings underscore the significant decrease in VL observed in both treatment groups over time, indicating the effectiveness of TLE + TLD and TLD alone in suppressing HIV replication and reducing VL levels. Despite some fluctuations, the overall trend suggests a favorable response to treatment, with patients experiencing substantial reductions in VL, particularly by 2020 and 2022.

Overall, the data advocate for the clinical significance of both TLE+TLD and TLD alone in achieving virological suppression and controlling disease progression in patients living with HIV. The findings highlight the importance of early initiation and adherence to antiretroviral therapy in effectively managing HIV infection and improving long-term clinical outcomes.

Discussion

This study aimed to assess the impact of newly introduced highly active antiretroviral therapy (HAART) on CD4 count, VL, WHO clinical stage, BMI, and weight in individuals diagnosed with HIV. The current standard practice in HIV treatment involves initiating HAART immediately upon positive screening results while obtaining baseline values for clinical assessment.

The comprehensive analysis of 261 HIV-infected patients provided valuable insights into various demographic patterns, modes of transmission, and treatment outcomes within the studied population. The relatively equal gender distribution and broad age range underscored the prevalence of HIV across different age groups and genders, emphasizing the need for tailored interventions across diverse demographics. Heterosexual transmission emerged as the predominant mode, highlighting the importance of targeted prevention efforts. Additionally, instances of mother-to-child transmission, MSM, and blood transfusion indicated the diverse pathways of HIV transmission, necessitating multifaceted prevention strategies.

The analysis of treatment outcomes revealed promising results associated with the TLD regimen compared to TLE. Patients on TLD exhibited higher median BMI and CD4 count, indicating potential improvements in metabolic health and immune function, respectively, which gives insight into antiretroviral therapy. The transition from TLE to TLD was also associated with significant viral load suppression, demonstrating the efficacy of TLD in controlling HIV replication and reducing transmission risk. These findings align with previous research[24,27], reaffirming the efficacy of dolutegravir (DTG) as a potent inhibitor of HIV integration. DTG plays a crucial role in impeding the integration of the virus into host cells by inhibiting the strand transfer process of retroviral DNA. As a result, DTG demonstrates a substantial genetic barrier against the development of drug resistance, which has already been proven the antiretroviral drug (increasing the CD4 count and suppressing viral load) In contrast, efavirenz shows suboptimal suppression of viral load, attributed to its lower genetic barrier against the emergence of drug-resistant virus variants.[25,26,28]

Moreover, the transition from TLE to TLE+TLD regimen demonstrated significant clinical implications. Patients on TLE+TLD exhibited higher CD4 counts and undetectable viral loads compared to those solely on TLE. This suggests a substantial improvement in immune function and effective viral suppression with the combined regimen.

Furthermore, the transition to TLE+TLD was associated with notable increases in BMI and weight, indicating potential benefits in metabolic health and nutritional status.

The subset analysis of patients initiating direct TLD therapy as a first-line intervention further underscored the clinical benefits of TLD. Significant improvements in CD4 counts, viral load suppression, and weight management were observed post-TLD initiation, highlighting the efficacy of TLD as a first-line treatment option, which is similar to the study conducted by Tamrakar R *et al.*, 2022.[29]

Significantly, a considerable number of participants exhibited a median weight gain of 4.6 kg upon transitioning to DTG. These results were consistent in a prior investigation examining weight changes following the initiation of antiretroviral therapy with DTG.[30,31] Notably,

approximately half of the participants experienced a median body weight gain of at least 2.0 kg. An increase in median BMI was noted among 116 patients transitioning from the time of diagnosis to when they were on TLD therapy. This data, obtained from a previous study, also included a comparison of BMI medians between patients on efavirenz and those on TLD.[32,33]

Additionally, the comparison of WHO clinical stage changes between patients receiving TLE+TLD and TLD alone revealed notable patterns in clinical progression. Both groups exhibited stability in stage I, with transitions to lower stages observed, indicating favorable clinical outcomes with appropriate treatment interventions. These results align with a prior study analyzing the same dataset, which similarly found that the majority of participants were in clinical stages I and II (67.41 and 15.73%, respectively).[34]

Furthermore, the comparison of CD4 count and viral load between patients initially treated with TLE+TLD and those on TLD alone demonstrated the effectiveness of both regimens in boosting immune function and suppressing HIV replication over time.

Overall, these findings emphasize the clinical efficacy of integrating dolutegravir into conventional therapeutic regimens for HIV management. The observed improvements in immunological, virological, and metabolic parameters highlight the importance of optimizing antiretroviral treatment strategies to enhance overall health and quality of life for individuals living with HIV.

Conclusion

The study findings reveal compelling evidence of the positive impact associated with initiating the recently introduced triple regimen, tenofovir/lamivudine/dolutegravir (TLD), in managing HIV patients. Notably, our results demonstrate consistent enhancements across various clinical parameters, indicating the effectiveness of TLD in improving patient outcomes. Of particular significance is the robust viral suppression observed across the diverse patient populations included in the study, suggesting the regimen's efficacy in controlling HIV replication.

These findings underscore the potential of TLD as a valuable addition to conventional HIV treatment strategies, offering not only improved efficacy but also sustained therapeutic benefits. By showcasing its ability to maintain viral suppression and enhance clinical outcomes, TLD emerges as a promising option for optimizing HIV management. However, to further solidify these findings and ensure their long-term applicability, additional research and comprehensive follow-up studies are warranted. Such endeavors will not only validate the encouraging outcomes observed in this study but also contribute to refining and optimizing HIV treatment protocols in clinical practice.

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