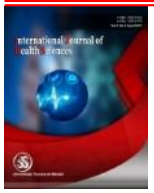


International Journal of Health Sciences

Available online at www.sciencescholar.us
Vol. 10 No. 2, August 2026, pages: 204-212
E-ISSN: 2550-696X
https://doi.org/10.53730/ijhs.v10n2.16008

Emergence of Resistance to Dolutegravir in Children in Senegal: A Report on the First Two Cases in the Thies Region

Fatou Sene [a], Malick Fall [b], Abdoul Magib Cissé [c], Oumar Diop [d], Anna Ndong [e] Adjaratou Aissatou Ba [f], Mbengue Fall [g], Sokhna Niang [h], Amady Sy [i], Adja Fatou Mbodji [j], Aminata Diop [k], Moussa Camara [l], Halimatou Diop-Ndiaye [m]

Manuscript submitted: 27 May 2026, Manuscript revised: 18 July 2026, Accepted for publication: 09 August 2026

Corresponding Author [a]

Keywords

Adolescents;
DTG resistance;
HIV;
Thiès;
viral load;

Abstract

In Senegal, despite the widespread implementation of pediatric antiretroviral therapy (ART), biological outcomes among children and adolescents remain suboptimal. The objective of this study was to evaluate biological monitoring and determine the antiretroviral drug resistance profile among children and adolescents receiving routine HIV care in the Thies region. This was a descriptive and analytical cross-sectional cohort study from January 2021 to December 2023, including children and adolescents aged 0–19 years, living with HIV, who had been receiving ART for at least six months, were regularly followed up, and had undergone three viral load assessments at months 12, 24, and 36. Genotypic resistance testing was performed in 18 children/adolescents. Cases of dolutegravir (DTG) resistance were identified in two HIV-infected adolescents in Senegal. In Case 1, mutations were identified at eleven positions, five of which were associated with drug resistance: E138K, G118R, M184V, M41L, and T215Y. In Case 2, mutations were detected at eleven positions, seven of which were associated with resistance: E138K, G140A, S147G, Q148R, M184V, T215F, and M41L. Although dolutegravir has demonstrated a high genetic barrier to resistance, routine and large-scale surveillance of primary resistance should be implemented to ensure the long-term effectiveness of DTG-based regimens.

[a] Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal and Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal
[b] Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal
[c] Department of pediatrics, Mbour Hospital, Mbour, Senegal
[d] Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal
[e] Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal
[f] HIV Reference Laboratory in Senegal, Dakar, Senegal
[g] HIV Reference Laboratory in Senegal, Dakar, Senegal
[h] HIV Reference Laboratory in Senegal, Dakar, Senegal
[i] Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal
[j] Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal
[k] Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal
[l] Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal
[m] HIV Reference Laboratory in Senegal, Dakar, Senegal

Contents

1 Introduction

The class of integrase inhibitors (INIs) has been among the most commonly prescribed antiretrovirals since 2019, with dolutegravir (DTG) leading the way. Despite their high efficacy, it is known that resistance to INIs can develop, leading to treatment failure. To date, mutations have been associated with INI resistance, although many of these are considered to be polymorphisms (De Clercq, 2009).

In 2019, the WHO recommended the use of DTG in adults and adolescents living with HIV (PLHIV) due to the development of resistance to non-nucleoside reverse transcriptase inhibitors, its high genetic barrier and its good tolerability. The development of a low-cost, single-tablet co-formulation combining tenofovir, lamivudine and dolutegravir, suitable for use from a body weight of 30 kg, has enabled the large-scale roll-out of DTG for both treatment initiations and pre-treated patients (Aboud et al., 2019).

In West Africa, people living with HIV are a population particularly at high risk of virological failure, especially in rural areas. In Senegal, for example, in 2016 the rate of virological failure could reach as high as 69% in rural areas, whereas it was less than 20% in paediatric hospitals in the capital (Kebe et al., 2013; Cissé et al., 2019). In this context, the transition to DTG, which began in 2020 among PLHIV who had been treated for years with often suboptimal regimens and without regular viral load monitoring, raises concerns about the emergence of DTG resistance and necessitates long-term clinical and virological monitoring (World Health Organization, 2022; Vitoria et al., 2018). We report the case of two adolescents with virological failure who exhibited resistance to DTG, a finding observed for the first time in Senegal, in the Thies region.

2 Materials and Methods

Both patients underwent three viral load tests over the past three years, from January 2021 to December 2024, at the laboratory of the El Hadji Amadou Sakhir Ndieguene Regional Hospital Center in Thies, using the Cobas AmpliPrep/CobasTaqman 48 platform (Roche).

Genotyping was performed on the protease (PR), reverse transcriptase (RT), and integrase (IN) genes using the Applied Biosystems™ HIV-1 Genotyping Kit (Thermo Fisher Scientific) and SeqStudio Genetic

Analyser (Thermo Fisher Scientific) at the National HIV Reference Laboratory in Senegal (LBV). Analysis of sequences and resistance mutations was carried out using the Recall/HIV Drug Resistance Database.
Genetic analysis of the integrase (IN) gene and the protease and reverse transcriptase (PROT/RT) gene was performed (simultaneously) on populations sensitive and resistant to NUC (Nucleoside Reverse Transcriptase Inhibitors) and NNUC (Non-Nucleoside Reverse Transcriptase Inhibitors), and a population resistant to all three (NUC, NNUC and IN). The reconstruction of maximum likelihood phylogenetic trees aims to minimise the total length of the tree and uses the Kimura-2-P model (= 2 parameters), (Kimura, 1980).

COMMENTS

Case No. 1
BD, now aged 17, has been under care since the age of 21 months (May 2009), amounting to 187 months of follow-up, following a perinatal infection. His CD4 count at that time was 960 cells/mm^3 (11%). His first ART treatment began at the same time, based on AZT/3TC/NVP. This initial regimen was changed in February 2010 (after 9 months) to D4T/3TC/EFV, probably due to AZT toxicity (anaemia at 6.5 g/dl), before reverting to the original regimen. The duration of this change in regimen was not specified. The first available viral load (VL) was obtained in March 2015, at 71 weeks of follow-up following the observation of clinical failure with WHO stage 3 symptoms. The viral load (VL) was then 34,000 copies/ml. The genotyping test carried out at the same time had shown resistance to EFV/NFV, high-level resistance to 3TC/FTC, and intermediate resistance to ABC and AZT, whilst D4T and DDI remained sensitive. These last two drugs were withdrawn from the current regimens. Resistance to protease inhibitors (PIs) had not been assessed. A second-line antiretroviral therapy (ART) regimen was introduced in July 2016, based on TDF/3TC/LPV/r. Since December 2020, following the introduction of DTG, the patient has been on TDF/3TC/DTG (TLD).

In terms of the wider context, the mother, who was being treated at the same facility, never disclosed her condition or that of her son to the father or other family members. The adolescent reported strained relationships and stigmatisation within his own family, as well as difficulties at school. Furthermore, during his stays in the village with his father, who was unaware of his illness, our patient did not take his medication regularly.

This patient's care was thus marked by frequent interruptions in treatment and poor adherence to ART. He experienced several episodes of illness: *Candida albicans* oesophagitis, diarrhoea and chronic dermo-epidermitis. Disclosure of his HIV status did not significantly improve his adherence to ARVs. An episode of delirium was observed in 2021. Psychological support was subsequently provided, but on an irregular basis (two contacts).

Case No. 2
The second case is an 11-year-old boy, who has been under follow-up for 132 months. HIV infection was diagnosed on 26 September 2016, at the age of 4, following the presentation of multiple abscesses, parotitis and chronic diarrhoea. ART based on AZT/3TC/NVP was initiated one week later (3 October 2016), although no CD4 count was available. After six months of relatively regular follow-up (October 2016 to March 2017), signs of disease progression (chronic parotitis, pyoderma and recurrent diarrhoea) were observed, and an initial viral load test returned a result of 49,600 copies/ml. He was lost to follow-up again for over two years and re-identified in May 2019. A new regimen based on ABC/3TC/Lr was introduced on 3 May 2019, but without success. Despite this new protocol, signs of disease progression are still noted: active molluscum contagiosum, polyadenopathy and episodes of recurrent diarrhoea. A new viral load test returned a result of 162,000 copies/ml. Patient education (PE) and the counselling process began, and treatment with ABC/TDF/DTG (TLD) was initiated on 18 August 2020, following the introduction of DTG into ART regimens as recommended by the national program.

This patient is the last and only infected child in a family of four. His mother was diagnosed shortly after he was weaned. Both parents are also infected; they are divorced and receiving care at another facility. The father has never been involved in his care. The mother looks after her children alone and lives in a large family compound, terrified that her status and that of her son will be revealed. Both patients are currently on the TDF/3TC/LPVr regimen. The second patient was fully informed of his status in December 2024.

3 Results and Discussions

3.1 Results

1. Viral load and genotyping results

- **CASE I**

The viral load measured in 2021 was 41,000 copies/ml, and that measured at M43 was 2,710 copies/ml. The most recent viral load was 6,150 copies/ml in 2024. Thus, viral load levels have remained undetected (> 1,000 copies/ml) throughout the last four years of follow-up. The three VL measurements obtained over three years indicate virological failure. Genotyping was performed on the sample (Case I). In the RT gene, the mutations associated with NRTIs were the 'thymidine analogue mutations' (TAMs) M41L and T215Y, conferring resistance to AZT, and the M184V mutation associated with resistance to 3TC/FTC. For NNRTI, the A98G and K238T mutations were noted, with high levels of resistance to NVP, intermediate resistance to EFV, and low resistance to doravirine and rilpivirine. No resistance mutations were observed for PIs, but major and cross-resistance to all integrase inhibitors was noted with the mutations G118R and E138K. (see Table I).

- **CASE II**

After having his viral load tested in 2021, the patient was lost to follow-up and re-identified in April 2023. The viral load was measured at 44,638 copies/ml. The notification process was resumed and completed in December 2024, and the TLD was resumed. Viral load monitoring in 2024 revealed virological failure with a viral load of 90,714 copies/ml and resistance to DTG (see table).

Genotyping was performed on the sample (Case II). In the RT gene, the mutations associated with NRTIs were the 'thymidine analogue mutations' (TAMs) M41L and T215Y, conferring resistance to AZT, and the M184V mutation associated with resistance to 3TC/FTC. For NNRTIs, the A98G and K238T mutations were noted, with high levels of resistance to NVP, intermediate resistance to EFV, and low resistance to doravirine (DRV) and rilpivirine (RPV). (Table I).

2. Results of genetic testing

Table 2 presents a detailed assessment of genetic structure between populations, using genetic distances and a genetic differentiation index (FST or similar). The results reveal a degree of divergence that goes beyond simple nucleotide variability. The genetic distance between RESISTANT_IN and Controls (35.564) and between SENSITIVE_IN and Controls (25.384) reaches very high values.

The phylogenetic tree of the integrase (IN) gene reveals a clear and robust pattern of evolutionary relationships between the sequences. The tree shows a major, well-supported division (99–100% bootstrap) into two main clades. All sequences in the study (sensitive and resistant) cluster within the same clade, whilst the two control sequences (A3.SN.01. DDI579.AY521629 and A3.SN.01. DDJ369.AY521631) form a distinct sister clade. This visual separation confirms the extremely high genetic distances calculated between the study groups and the controls.

3.2 Discussions

Cases of resistance to DTG have been reported among HIV-infected adults in Cameroon and South Africa (Loosli et al., 2023; Mahomed et al., 2020). DTG is an INI with a high genetic barrier and is also well tolerated, making it the cornerstone of treatment regimens rapidly adopted by the National Program on HIV/AIDS (PNLS). Its roll-out has raised high hopes for controlling the pandemic (World Health Organization, 2022).

However, access to regular viral load testing has long been a challenge at certain treatment sites. In his 2022 thesis, Diokh reported the following findings in the Thies region (n=170): 47.7% of children had undergone viral load testing within 2 years, and 37.7% within 3 years. Only 2% of children had two annual viral load tests (Diokh, 2022). However, the fact that the viral load value for Case I has fallen since the first measurement supports the theory that a mutated virus struggles to replicate.

Our two cases highlight the impact of not disclosing one's HIV status within families, self-stigmatisation and socio-cultural constraints in our context. Indeed, these situations constitute a major obstacle to good adherence and regular follow-up (Mbhele et al., 2021).

Regarding Case No. 1, using the sequence interpretation algorithms currently available (ANRS, Stanford HIVdb and Rega), we identified the presence of mutations at nine positions, five of which were associated with resistance, notably E138K, G118R, M184V, M41L and T215Y. The mutations L74F, A98G, K238T and S68G were classified as accessory resistance mutations by the HIV Drug Resistance Database and the three interpretation algorithms (ANRS, Stanford and Rega). In Case No. 2, we identified mutations at eleven positions, seven of which were associated with resistance, notably E138K, G140A, S147G, Q148R, M184V, T215F and M41L. The mutations T97A, A98G, K238T and S68G were classified as accessory resistance mutations by the HIV Drug Resistance Database and the three interpretation algorithms (ANRS, Stanford and Rega) (Torres-Fernandez et al., 2022; McCluskey & Gandhi, 2025). The observed resistance to DTG could be explained by the fact that these children were not treatment-naïve patients and were therefore likely on monotherapy, as they already exhibited resistance to NNRTIs and NRTIs (Case No. 1: AZT+3TC+NVP/TDF+3TC+DTG; Case No. 2: AZT/3TC/NVP-ABC/3TC/DTG).

This study depicts the emergence of antiretroviral resistance as a phenomenon of micro-scale speciation. Under therapeutic pressure, the virus does not merely acquire a few survival mutations; it enters a state of accelerated and divergent evolution that frees it from normal functional constraints, generates hypervariability, and genetically isolates the new resistant populations. Very high indices of genetic differentiation (close to 1) demonstrate that the resistant populations, particularly RESISTANT_IN, now constitute distinct and isolated genetic entities. They have diverged significantly from the local circulating viral pool and are now following parallel evolutionary trajectories (Murphy et al., 2010).

4 Conclusion

The genotyping results remain alarming regarding the resistance to dolutegravir found in these two patients. The resistance observed in these children is the result of extensive, complex, and multifocal viral adaptation, illustrating HIV's ability to evolve in response to therapeutic challenges. Surveillance of this primary resistance should be carried out regularly and on a large scale. Although DOLUTEGRAVIR has demonstrated a high genetic barrier to resistance, we must remain highly vigilant and expand the study to a national level to ensure better management of associated resistances, particularly in children and adolescents.

Acknowledgments
We are grateful to two anonymous reviewers for their valuable comments on the earlier version of this paper.

References

Aboud, M., Kaplan, R., Lombaard, J., Zhang, F., Hidalgo, J. A., Mamedova, E., ... & Smith, K. (2019). Dolutegravir versus ritonavir-boosted lopinavir both with dual nucleoside reverse transcriptase inhibitor therapy in adults with HIV-1 infection in whom first-line therapy has failed (DAWNING): an open-label, non-inferiority, phase 3b trial. *The Lancet infectious diseases*, *19*(3), 253-264.

Cissé, A. M., Laborde-Balen, G., Kébé-Fall, K., Dramé, A., Diop, H., Diop, K., ... & Touré-Kane, C. (2019). High level of treatment failure and drug resistance to first-line antiretroviral therapies among HIV-infected children receiving decentralized care in Senegal. *BMC pediatrics*, *19*(1), 47.

De Clercq, E. (2009). Anti-HIV drugs: 25 compounds approved within 25 years after the discovery of HIV. *International journal of antimicrobial agents*, *33*(4), 307-320. https://doi.org/10.1016/j.ijantimicag.2008.10.010

Diokh J. (2022). Bilan global de la prise en charge des enfants et adolescents vivant avec le VIH dans la région de Thiès. Thiès : Unité de Formation en Science de la Santé, Université Iba Der Thiam. Anneé. 80

Kebe, K., Thiam, M., Diagne Gueye, N. R., Diop, H., Dia, A., Signate Sy, H., ... & Toure Kane, C. (2013). High rate of antiretroviral drug resistance mutations in HIV type 1-infected Senegalese children in virological failure on first-line treatment according to the World Health Organization guidelines. *AIDS research and human retroviruses*, *29*(2), 242-249.

Kimura, M. (1980). A simple method for estimating evolutionary rates of base substitutions through comparative studies of nucleotide sequences. *Journal of molecular evolution*, *16*(2), 111-120.

Loosli, T., Hossmann, S., Ingle, S. M., Okhai, H., Kusejko, K., Mouton, J., ... & Kouyos, R. D. (2023). HIV-1 drug resistance in people on dolutegravir-based antiretroviral therapy: a collaborative cohort analysis. *The Lancet HIV*, *10*(11), e733-e741.

Mahomed, K., Wallis, C. L., Dunn, L., Maharaj, S., Maartens, G., & Meintjes, G. (2020). Case report: Emergence of dolutegravir resistance in a patient on second-line antiretroviral therapy. *Southern African Journal of HIV Medicine*, *21*(1), 1-4.

Mbhele, N., Chimukangara, B., & Gordon, M. (2021). HIV-1 integrase strand transfer inhibitors: a review of current drugs, recent advances and drug resistance. *International journal of antimicrobial agents*, *57*(5), 106343. https://doi.org/10.1016/j.ijantimicag.2021.106343

McCluskey, S. M., & Gandhi, M. (2025). Predictors of treatment-emergent resistance to dolutegravir. *The Lancet HIV*, *12*(9), e660-e663.

Murphy, D. A., Lam, P., Naar-King, S., Harris, D. R., Parsons, J. T., Muenz, L. R., & Adolescent Medicine Trials Network for HIV/AIDS Interventions. (2010). Health literacy and antiretroviral adherence among HIV-infected adolescents. *Patient education and counseling*, *79*(1), 25-29. https://doi.org/10.1016/j.pec.2009.07.014

Torres-Fernandez, D., Jiménez de Ory, S., Fortuny, C., Sainz, T., Falcón, D., Bernal, E., ... & Prieto, L. (2022). Integrase inhibitors in children and adolescents: clinical use and resistance. *Journal of Antimicrobial Chemotherapy*, *77*(10), 2784-2792.

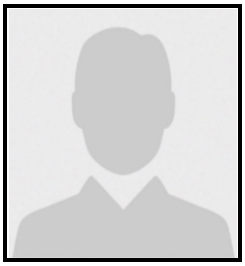
Vitoria, M., Hill, A., Ford, N., Doherty, M., Clayden, P., Venter, F., ... & Domanico, P. L. (2018). The transition to dolutegravir and other new antiretrovirals in low-income and middle-income countries: what are the issues?. *Aids*, *32*(12), 1551-1561.

World Health Organization. (2022). *Sentinel surveys of acquired HIV resistance to dolutegravir among people receiving dolutegravir-containing antiretroviral therapy*. World Health Organization.

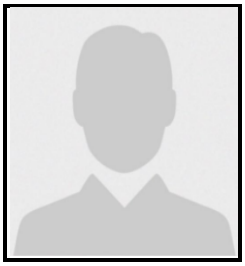
World Health Organization. (2022). *Stratégies mondiales du secteur de la santé contre, respectivement, le VIH, l'hépatite virale et les infections sexuellement transmissibles pour la période 2022-2030*. World Health Organization.

Biography of Authors

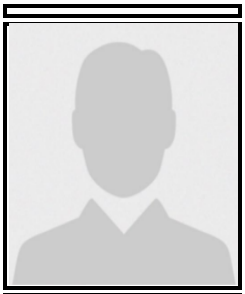
Fatou Sene
Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal and Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal
Email: fatoukinesene3@gmail.com



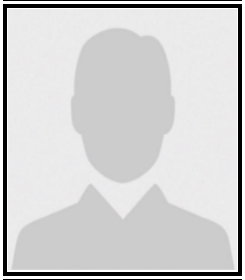
Malick Fall
Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal



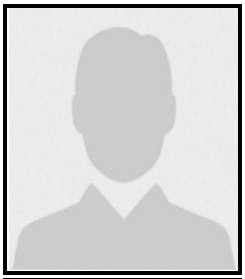
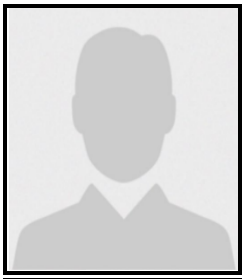
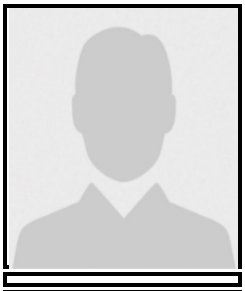
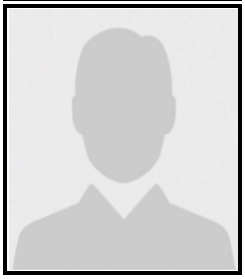
Abdoul Magib Cissé
Department of pediatrics, Mbour Hospital, Mbour, Senegal

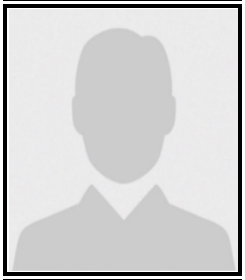


Oumar Diop
Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal

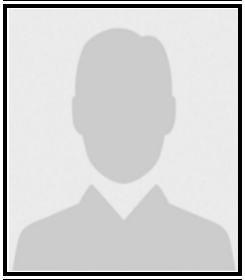


Anna Ndong
Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal

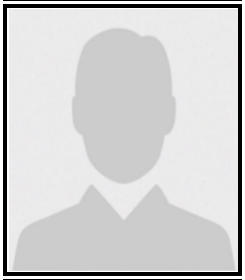
	**Adjaratou Aissatou Ba** HIV Reference Laboratory in Senegal, Dakar, Senegal
	**Mbengue Fall** HIV Reference Laboratory in Senegal, Dakar, Senegal
	**Sokhna Niang** HIV Reference Laboratory in Senegal, Dakar, Senegal
	**Amady Sy** Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal
	**Adja Fatou Mbodji** Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal



Aminata Diop
Laboratory at the El Hadji Amadou Sakhir Ndieguene Regional Hospital in Thiès, Thiès, Senegal



Moussa Camara
Department of Animal Biology, Faculty of Science and Technology, Cheikh Anta Diop University, Dakar, Senegal



Halimatou Diop-Ndiaye
HIV Reference Laboratory in Senegal, Dakar, Senegal