Life-Saving but Risky: Antiretroviral Therapy and Rising Diabetes Risk in Rural South Africa

A Short storytelling based on the peer-reviewed paper:

Bam, N.E., Mabunda SA, Ntsaba J, Apalata T, Nomatshila SC, and Chitha W (2020) The association between HIV tri-therapy with the development of Type-2 Diabetes Mellitus in a rural South African District: A case-control study. ***PLoS ONE*** 15(12): e0244067. https://doi.org/10.1371/journal.pone.0244067

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A Double-Edged Sword of Progress

Antiretroviral therapy (ARVs), especially in the form of combination regimens (cARVs), has been one of the greatest medical achievements of our time. For people living with HIV/AIDS (PLWHIV), these drugs transformed a once fatal illness into a manageable chronic condition, giving hope and extending life expectancy.

Yet, this progress comes with a new challenge: an increased risk of type-2 Diabetes Mellitus (DM). This study, conducted in a rural South African district, provides compelling evidence that cARVs are strongly linked to the development of diabetes, underscoring the need for vigilance in long-term HIV care.

Which Drugs Pose the Greatest Risk?

Not all ARVs carry the same risk. While the fixed-dose combination (FDC) of tenofovir (TDF), emtricitabine (FTC), and efavirenz (EFV), South Africa's standard first-line treatment, was relatively safer, other regimens showed alarming associations with diabetes:

Protease Inhibitors (PIs):

- Patients on AZT/3TC/lopinavir (LPV) were 31 times more likely to develop diabetes.
- Patients on AZT/3TC/ritonavir (RTV) were 21 times more likely.
- Both results were highly significant ($p<0.0001$).

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs):

Zidovudine (AZT): Patients on AZT/3TC/EFV were 9.4 times more likely to be diabetic ($p<0.0001$).

Stavudine (D4T): Patients on D4T/3TC/EFV were 2.5 times more likely ($p=0.003$).

Interestingly, the AZT/3TC/NVP regimen showed no significant association, though this was likely due to a very small sample size.

Time Matters: The Longer on ARVs, the Higher the Risk

Duration of ARV exposure emerged as a critical factor:

- 6–10 years on ARVs: 3.4 times more likely to develop diabetes.
- Over 10 years: 4.3 times more likely.

Notably, 61% of diabetic cases were diagnosed after starting ARVs, strongly suggesting a treatment-related cause. In addition, diabetic patients were three times more likely to report ARV-related complications compared to non-diabetics.

What This Means for South Africa

South Africa runs the world's largest ARV program. As more PLWHIV live longer, the overlap between HIV and chronic conditions like diabetes is growing rapidly. This study warns that unless addressed, the health system will face a surge of multi-morbidity cases.

The findings call for:

- Careful use of high-risk drugs (AZT, D4T, LPV, RTV), reserving them for patients who fail safer regimens.
- Exploration of alternatives like Abacavir (ABC) or second-line PIs such as Darunavir (DRV) and Atazanavir (ATV).
- Routine monitoring of metabolic health among patients on cARVs.
- More prospective studies to uncover mechanisms, predict risk, and identify ARV regimens that minimize diabetogenic effects.

The Takeaway

ARVs remain a lifeline, but survival must go hand in hand with quality of life. With careful planning, early monitoring, and informed drug choices, South Africa can continue to lead in HIV/AIDS care while protecting patients from the growing burden of diabetes.