In-silico characterisation of reverse transcriptase gene of HIV-1 Drug Resistant Strains from Southern India

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ABSTRACT

Introduction: HIV-positive patients in India are experiencing drug resistance due to a lack of adherence to Antiretroviral Therapy (ART). ART regimens currently in use are challenged by drug resistance that occurs as HIV accumulates key mutations. In the present study, we examined naïve ART patients from ART centres, Government Hospitals, Salem district, Tamil Nadu where subtype C is highly prevalent and reverse transcriptase gene sequences were used for modelling protein structure and molecular docking. **Objective:** To characterize the HIV-1 drug-resistant viruses by the *in-silico* molecular docking method. **Materials and methods:** Of 33 first-line ART failure cases we took the reverse transcription sequences of 2 for further analysis. For docking studies, the NRTI drugs Stavudine, Tenofovir, Zidovudine and Lamivudine were selected against GMKMC-4 and GMKMC-17 HIV proteins. The docking studies are in concert with the *in-silico* drug ligand interactions of four NRT1 drugs with the GMKMC-4 and 17 HIV proteins. Docking scores (binding energies) and Stanford DR online database (Stanford University, CA, USA) to predict which mutants would affect the docking scores of different reverse transcriptase inhibitors based on RT sequences of two isolates of first-line therapy failures. **Results and conclusion:** The observed binding energies against GMKMC-17 protein were Stavudine –6.5122 kJ/mol, Tenofovir –7.1293 kJ/mol, Lamivudine –5.0554 kJ/mol and Zidovudine –5.2476 kJ/mol. While the energy binding values against GMKMC-4 protein were Tenofovir –6.3462 kJ/mol, Stavudine –3.2453 kJ/mol, Zidovudine –4.1982 and Lamivudine –2.4572 kJ/mol. *In-silico* evaluations show that Tenofovir inversely correlates with the level of drug resistance. The present study shows that computational modelling could be effectively used for drug design.