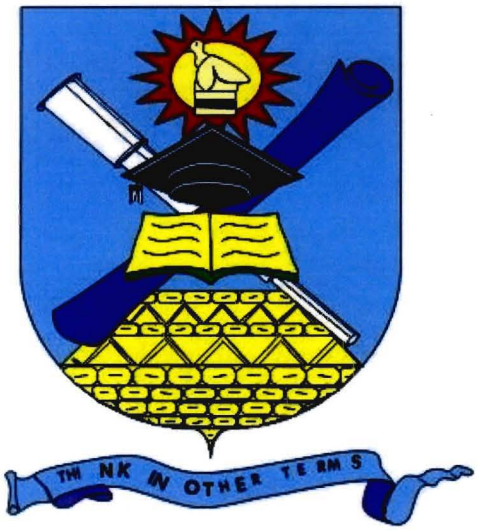

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CYP3A5 PHARMACOGENETICS IN HIV POSITIVE ZIMBABWEAN ADULTS: A WINDOW INTO PERSONALIZED MEDICINE

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ABSTRACT

Background; The field of pharmacogenetics is targeted at understanding the impact of the genetic profiles of individuals on their response to medication with the goal of enabling personalised treatment. Pharmacogenetic research is motivated by the observation that current medications, given in standard doses, result in adverse drug reactions (ADRs) in some patients mainly due to polymorphisms in drug metabolism enzymes such as the cytochromes P450. CYP3A5 is a polymorphically expressed drug metabolizing enzyme and SNPs in the gene are a cause for varied interethnic and inter-individual metabolism of CYP3A5 substrates. *Aim;* The study sought to determine the allele frequencies of the CYP3A5*3 SNP in black HIV positive Zimbabwean adults on nevirapine based antiretroviral therapy using PCR-RFLP and TaqMan® real-time PCR so as to outline population distribution, recommend a robust genotyping technology for use in local laboratories and determine any association with ADRs. *Materials and methods;* DNA for the study was obtained from the AiBST biobank. PCR-RFLP and TaqMan® real-time PCR were used to genotype the study samples. Logistic regression modelling was used to determine any associations between genotype and ADRs. *Results;* The frequencies of major CYP3A5 alleles were analysed and 86% of the Zimbabwean adults were identified as carriers of the wild type allele whereas 14% carry the mutant allele. There was >99% concordance between PCR-RFLP and TaqMan® real-time PCR in genotyping CYP3A5 polymorphisms in the study population. Logistic regression modelling of observed phenotypic traits for nevirapine induced skin hypersensitivity determined that females homozygous for CYP3A5*1 on stavudine, lamivudine and nevirapine therapy were less likely to develop skin hypersensitivity ($\widehat{OR} = 0.09$, $p = 0.0006$). *Conclusions;* The frequency of CYP3A5 allelic variants in our sample cohort of the Zimbabwean population compares well with reported data on African populations. PCR-RFLP and TaqMan® real-time PCR are robust technologies for genotyping SNPs in research or diagnostic laboratories, both with comparable results. There is need for further research to define associations between CYP3A5 genotype and nevirapine related ADRs.