# A study of the clinically important *CYP2C19* gene variants in the Sri Lankan Population

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**Background & Objectives:** *CYP2C19* is the most polymorphic gene belonging to cytochrome P450 superfamily of drug metabolizing enzymes. *CYP2C19* catalyzes the metabolism of a range of clinically important drugs such as anti-epileptics (diazepam, phenobarbitone), antidepressants (amitriptyline clomipramine), the antiplatelet drug clopidogrel, and anti-ulcer proton pump inhibitors (omeprazole, lansoprazole). Three of its variants, *CYP2C19*2*, *CYP2C19**3 and *CYP2C19*17*, are considered to be clinically important. *CYP2C19*1* is the wild type allele and individuals homozygous for this allele exhibit the normal metabolizer phenotype, with a normal enzyme activity. Phenotypically, *CYP2C19*2* and *CYP2C19*3* are associated with poor metabolizers (PM) and *CYP2C19*17* is associated with ultra-rapid metabolizers (UM). The objective of the study was to determine the frequency of these alleles in the Sri Lankan population.

**Method (s) and Results:** Peripheral blood samples were collected from individuals (n = 100) referred to the Human Genetics Unit, University of Colombo, for genetic screening retrospectively following ethical clearance. Genotyping was achieved by the T-ARMS-PCR method. Results were confirmed by PCR-RFLP assays and validated by Sanger Sequencing. The observed and expected frequencies were calculated using Hardy-Weinberg equation. Genotype analysis revealed that the allele frequencies of *CYP2C19*2*, *CYP2C19*3* and *CYP2C19*17* in the Sri Lankan population were 0.3, 0.01 and 0.2, respectively. Out of the 100 subjects, 30% were normal metabolizers (*CYP2C19*1/*1* genotype); while 37% were intermediate metabolizers *(*1*2, *2*/17, *3*/17*), 12% poor metabolizers *(*2/*2*), 19% rapid metabolizers *(*1/*17*), and 2% were ultra-rapid metabolizers *(*17/*17*). The expected frequencies of *CYP2C19* genotypes in Sri Lankan population had no significant deviation from the Hardy-Weinberg equilibrium ($p>0.05$).

**Conclusions:** We can predict from this data that 70% of patients would require consideration of alternative treatment or dose adjustment based on their genotype, for the aforementioned drug classes. Therefore, we recommend that testing for these alleles be started in Sri Lanka.

**Conflict of interest disclosure:** No conflicts of interest.

**Keywords:** *CYP2C19*, variants, Sri Lankan population, T-ARMS-PCR, pharmacogenomics