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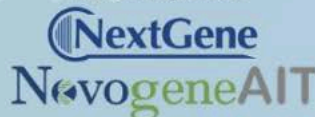
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Evaluation of Metformin Induced Gastrointestinal Adverse Drug Reaction with Organic Cation Transporter OCT1 Genetic Variation in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Background: Metformin is the first line agent in treating Type 2 Diabetes Mellitus (T2DM). It is widely prescribed due to its safety profile, which does not cause hypoglycemic episodes, cheap in cost and is also weight-neutral. However, it could cause gastrointestinal discomfort, which accounts for about 20-30% of the population. Studies suggested that the gastrointestinal discomfort might be contributed by the genetic variation of gene SLC22A1, which encodes for OCT1 transporter. The prevalence of gastrointestinal adverse drug reaction (ADR) of metformin among Malaysian population and its associated genetic variation has scarcely been investigated. This study aims to evaluate the prevalence of metformin induced gastrointestinal ADR among T2DM patients and its association with OCT1 transporter SLC22A1 genetic variations of R61C and M420del. **Methods:** This study employed point prevalence and retrospective case control design involving patients identified from the Electronic Medical Record (EMR) system of a teaching hospital from May 2021 to June 2022. Patients were classified as either tolerant or intolerant to metformin. A total of 235 patients who have met the inclusion criteria were included in the study. For genetic screening, 55 patients underwent peripheral blood sample collection. The samples were subsequently sent to iPROMISE, UiTM Puncak Alam for DNA extraction and Nanopore sequencing. **Results:** It was found out that 27 (11.5%) from 235 patients, were metformin intolerance. However, there was no significant association between R61C and M420del genetic variations with metformin induced gastrointestinal intolerance. Interestingly, the study identified two variants (rs1867351 and rs628031) that may warrant further investigation in future studies to better understand their phenotypic impact. **Conclusion:** The results indicate that within Malaysian population, R61C and M420del do not serve as reliable biomarkers for metformin induced gastrointestinal ADRs. Further investigation of broader pharmacogenetic markers may help identify clinically relevant risk alleles associated with metformin intolerance.

Keyword: Metformin-induce gastrointestinal adverse drug reaction; OCT1 genetic variation; type 2 diabetes