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Drug Transporters Polymorphism Among Indonesian Population: A Review

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Abstract

Genetic polymorphisms in drug transporters markedly affect drug absorption, distribution, and elimination, thereby contributing to interindividual variability in pharmacological responses. A comprehensive understanding of these genetic variations is essential for the advancement of personalized medicine, especially within genetically heterogeneous populations such as Indonesia.

Aims: This investigation seeks to elucidate the influence of drug transporter polymorphisms on therapeutic outcomes and their ramifications for personalized medicine in the Indonesian context. This study amalgamates existing research to furnish insights into genetic variations that impact drug metabolism, aiding the optimization of pharmacotherapy practices in Indonesia.

Methodology: A systematic literature review was performed utilizing the PubMed database, identifying studies published between 2013 and 2025 that pertain to drug transporter polymorphisms within the Indonesian cohort. The data extraction process concentrated on the pharmacokinetic and pharmacodynamic implications of genetic variations in pivotal transporters.

Results: A total of twelve studies were analyzed, predominantly focusing on SLC22A1, SLCO1B1, and ABCB1 polymorphisms in connection with the treatment of diabetes, cancer, epilepsy, hypercholesterolemia, and tuberculosis. The SLC22A1 Met420del variant was associated with modified metformin pharmacokinetics, while SLCO1B1 polymorphisms influenced statin metabolism, and ABCB1 variants were investigated concerning chemotherapy drug resistance. Nevertheless, inconsistent clinical significance was noted, attributable to limited sample sizes and discrepancies in methodologies.

Scientific Novelty: This study underscores the imperative to incorporate pharmacogenetic principles into Indonesia's healthcare framework while addressing challenges such as research funding, restricted access to diverse samples, and lack of pharmacogenetic knowledge among practitioners. This research uniquely consolidates evidence regarding genetic determinants that influence drug metabolism in Indonesia, thereby establishing a foundational basis for personalized medicine initiatives within a genetically diverse population.

Conclusion: Pharmacogenetics can optimize resources, decrease side effects, and increase treatment efficacy. Future initiatives should prioritize expanded research, public awareness, and governmental support to ensure the effective implementation of personalized medicine in Indonesia.

Keywords: pharmacogenetics; drug transporters; polymorphisms; personalized medicine.

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Introduction

Considering Indonesia's profound genetic diversity and its prominent contribution to individual differences in drug response, a more personalized therapeutic strategy is also warranted [1]. The population carries various polymorphisms in drug-metabolizing enzymes and transporters, which can affect pharmacokinetics and pharmacodynamics and have consequences for drug efficacy and safety [2, 3]. Differential expression of genetic markers, especially single nucleotide polymorphisms (SNPs), between ethnic groups can ultimately lead to differences in response to therapy and adverse drug reactions [4, 5]. These unique pharmacogenetic characteristics highlight the need for population-specific approaches in Indonesian clinical practice.

Functional Relevant Variants of drug metabolism pathway among the Indonesian population would be genotyped to provide a robust conclusion as studies such as polymorphisms of SLCO1B1 have revealed the identification of prevalent drug sensitive alleles [6], p450 enzyme, as well as wild type (wt) among the Sundanese in Indonesia (SLCO1B1 rs4149032), and a homozygous mutation of CYP3A5 wt among the Javanese and Sundanese cohort [7]. These results hold significant implications for treating diseases, including tuberculosis, cancer, diabetes, and cardiovascular diseases, which are developmental areas where pharmacogenomics can have an unambiguous and direct impact on therapeutic efficacy [7, 9]. Consequently, understanding allele distribution and clinical implications in these significant disease burdens is pivotal for tailoring individualized treatments in the Indonesian setting.

Further interindividual variation is introduced with the modulation of drug transporters and the metabolic enzymes that process drugs at the genetic, transcriptional, and post-transcriptional levels by environmental exposures, including pesticides [10, 11]. The expression and activity of transporters can be further regulated by genetic and non-genetic factors, including transcription factors, such as the nuclear hormone receptors, e.g., PXR and CAR [3, 12]. Such complexity underscores the multifactorial nature of drug response, necessitating a systems biology approach for accurate prediction models.

Pharmacogenomic initiatives like validating the Nala PGx Core® panel and the Biomedical and Genome Science Initiative (BGSi) are important milestones in Indonesia toward precision medicine [1, 13]. PharmFreq and other tools that map allele frequencies across populations [14] are critical for understanding genetic disparities and optimizing region-specific strategies. Nevertheless, the AIPG has encountered considerable challenges in the uptake of pharmacogenomics in Indonesia related to limited infrastructure, the inconsistent adaptation of policies, and inadequate awareness among clinicians [15,16]. Addressing these barriers will be essential to accelerate the clinical integration of pharmacogenomics across healthcare systems in Indonesia.

Despite the availability of global frameworks such as EMA and FDA [17]. Furthermore, the relevance also demonstrated its clinical relevance (e.g., transporter polymorphisms such as ABCB1 associated with delayed chemotherapy-induced nausea and vomiting), making it clear how genetic variation impacts drug response [18, 19]. Efflux and uptake transporters, e.g., OATP1B1, OCT1, and MATE1, are known to mediate significant drug-drug and drug-gene interactions, but studies remain sparse in the context of ethnic diversity [12, 20]. Therefore, expanding pharmacogenomic research in diverse Indonesian ethnic groups is crucial to bridging this knowledge gap and improving therapeutic equity.

Considering this context, characterizing drug transporter polymorphisms is critical for promoting equitable and efficient pharmacogenomic implementation in Indonesia's ethnically diverse population. This review intends to map the existing drug transporter polymorphisms in Indonesian populations and consequently find the gaps in this context needed to establish a rightful personalized treatment approach.

Research Problem

As a genetically diverse and developing nation, Indonesia has encountered considerable roadblocks to including pharmacogenetics in clinical settings. Several rationales exist for this phenomenon; however, a predominant concern is the limited understanding of polymorphisms in drug transporters, which play a crucial role in drug absorption, distribution, metabolism, and elimination. This lack of knowledge can modulate any differences in response to drugs, their therapeutic action and the risk of ADRs. The prevalence of ADRs in Indonesia has been reported to range widely between 0.9%–99%, based on the type of drug, dosage, and treatment duration in a systematic review report by [21]. Such high variability in the prevalence of ADR points to the complexity of drug response events in Indonesia, making it important to further explore genetic factors like transporter polymorphisms. Global pharmacogenetic studies on transporter polymorphisms, including SLC22A1 (OCT1) in metformin response, SLCO1B1 in statin-induced myopathies and ABCB1 in drug resistance have been undertaken; however, their clinical implications are still underutilized in Indonesian population due to the unavailability of population-specific studies.

Apart from scientific knowledge gaps, the implementation of pharmacogenetics in Indonesia is hampered by systemic barriers, including the high costs of research, limited access to genetic screening, and the absence of pharmacogenetic guidelines that address the population's needs. Genetic testing continues to be costly, precluding access to a substantial portion of the general public, especially in rural regions. There are no national laws regulating pharmacogenetic integration into healthcare in Indonesia. While initiatives (BGSi) plan to help genomic researchers, more programs must follow to transform discovery into clinical application. Thus, this study aims to fill in the gaps by compiling the available literature data on polymorphisms of drug transporters in individuals from Indonesia, identifying key genetic variations, and suggesting interventions for personalized medicine approaches that will improve drug safety, optimize the efficacy of treatment, and resulting in future pharmacogenetics policy.

Research Focus

This study aims to evaluate genetic polymorphisms of major drug transporters in the Indonesian population, especially SLC22A1 (OCT1), SLCO1B1, and ABCB1. These transporters are central to drug uptake, distribution, and elimination, thereby influencing therapeutic outcomes of many diseases. The aim is to elucidate the impact of these variations on drug pharmacokinetics and pharmacodynamics. This knowledge has implications in terms of therapeutic effect and safety and will help facilitate the practice of personalized medicine. Given the above, this study focuses on drug transporters that play significant roles in the treatment of common therapeutic areas or therapeutic areas that are frequently used in Indonesia, namely the diabetes drugs (i.e., metformin), hypercholesterolemia (i.e., statins), epilepsy (i.e., antiepileptics), and cancer (i.e., taxan chemotherapy and doxorubicin). This study conducted an extensive review of the literature on transporter polymorphisms and drug response in these conditions to provide insights into population-specific genetic variants that may affect drug receptor sensitivity and consequent adverse drug reaction (ADR) while also emphasizing the importance of genetic variation in drug response for optimal treatment in different populations.

Research Aim and Research Questions

To evaluate the available polymorphisms of drug transporters in the Indonesian population and analyze the association of the polymorphisms with drug response, therapeutic effectiveness, and safety. By studying SLC22A1 (OCT1), SLCO1B1 and ABCB1, this study aims to examine their role in therapeutic usages, such as diabetes in the form of metformin, hypercholesterolemia with statins, epilepsy in the form of antiepileptics, and lastly cancer in drugs meant for chemotherapeutics, such as paclitaxel and doxorubicin. The results of this study are expected to be used to help integrate pharmacogenetics into personalized medicine approaches in Indonesia by determining clinically relevant genetic variants that can be used in clinical settings to guide physicians on which medications should be prescribed to improve treatment efficacy and reduce the risk of ADRs. Moreover, this study focuses on identifying gaps in the relevant literature and barriers to implementation, then suggests recommendations on developing clinical guidelines to integrate pharmacogenetics into Indonesia's healthcare system.

Research Questions

1. What are the most common drug transporter polymorphisms found in the Indonesian population?

2. How do these polymorphisms influence the pharmacokinetics and pharmacodynamics of drugs used for therapies such as cancer, diabetes, epilepsy, hypercholesterolemia, and tuberculosis?

3. What is the relationship between genetic polymorphisms of drug transporters and clinical responses or adverse effects in the Indonesian population?

4. What are the primary challenges in integrating pharmacogenetics into Indonesia's healthcare system, and what solutions can be proposed?

5. How does Indonesia's genetic diversity influence the implementation of pharmacogenetics in personalized medicine?

To address these questions, this study aims to evaluate the available evidence on drug transporter polymorphisms in the Indonesian population, assess their clinical implications in drug response, and explore the potential of incorporating pharmacogenetics into Indonesia's healthcare system. The discoveries made through the project will serve as a reference point for subsequent research in pharmacogenetics, policies, and personalized medicine in the nation, thereby improving drug safety, effective treatment and efficiency in the health system.

Research Methodology

General Background

The genetics of drug transporters is an important aspect of the field of pharmacogenetics. However, polymorphisms in genetic variations (i.e., SNPs) play different roles in the absorption, distribution, metabolism and excretion of drugs. Given the extravagant ethnic diversity and interethnic marriages of Indonesia, localized pharmacogenetic data are required to determine the most relevant transporter polymorphisms and their clinical impact on this population. As SLC22A1 (OCT1) is globally significant to metformin response, and SLCO1B1 and ABCB1, respectively, for statin and chemotherapy drug resistance, the lack of Indonesian-specific data is a challenge for the application of pharmacogenetics in the clinical setting to approach precision medicine. The situation is compounded by the high cost of research, limited access to genomics data, inadequate infrastructure, and the lack of national pharmacogenetic guidelines, which leave clinicians dependent on foreign databases that may not reflect the genetics of Indonesia. To do this, the current study investigated and analyzed the polymorphisms of drug transporters (SLC22A1, SLCO1B1, and ABCB1) in the Indonesian population, as well as their physiology with respect to several drugs that are commonly used in the combined therapy, including metformin, statins, antiepileptics, and chemotherapy agents. In doing so, this study serves to uncover population-specific genetic variations, evaluate their influence on clinical efficacy, and advance the clinical implementation of pharmacogenetics within the Indonesian medical sector.

Sample / Participants / Group

Therefore, a systematic approach was used in this literature review, which was to select studies that report polymorphisms of drug transporters in the Indonesian population. The search is conducted on the PubMed database using a combination of keywords: ((“Membrane Transport Proteins”[Mesh]) AND (“Polymorphism, Genetic”[Mesh] OR “Polymorphism, Single Nucleotide”[Mesh] OR “Polymorphism, Single-Stranded Conformational”[Mesh])) AND “Indonesia”[Mesh]). The search focused on peer-reviewed studies published between 2013 and 2025 to ensure that all relevant studies, particularly the most recent ones, were included. All other study types were excluded, and the following eligibility criteria were applied to further refine the search results: (1) studies investigating genetic polymorphisms of drug transporters in the Indonesian population; (2) studies evaluating the effect of genetic polymorphisms of drug transporters on pharmacokinetics, pharmacodynamics, drug response or adverse drug reactions (ADRs); (3) studies written in the English language; and (4) studies that have the full-text available. Exclusion criteria included (1) publications that focused only on drug-metabolizing enzymes with no evaluation of drug transporters, (2) publications that reported only animal or in vitro data with no clinical or population information, and (3) review articles with no primary research findings. After applying relevance to research, a total of 28 studies from an initial 56 publications were identified as meeting the inclusion criteria. For final selection, more specific criteria were used, favoring studies with complete genotype-phenotype correlation and an investigation of polymorphisms of SLC22A1, SLCO1B1, and ABCB1 because those transporters are clinically relevant with their corresponding therapies in diabetes (metformin), hypercholesterolemia (statins), epilepsy (antiepileptics), and oncology (chemotherapy agents like paclitaxel and doxorubicin). Thus, after a critical appraisal of the study design, sample size, and clinical applicability, a total of 14 studies have been included that potentially offered various important information on drug transporter gene polymorphisms and the implications for pharmacogenetics in the Indonesian population. Thus, this methodology allowed us to systematically review the spectrum of literature relevant to the synthesis.

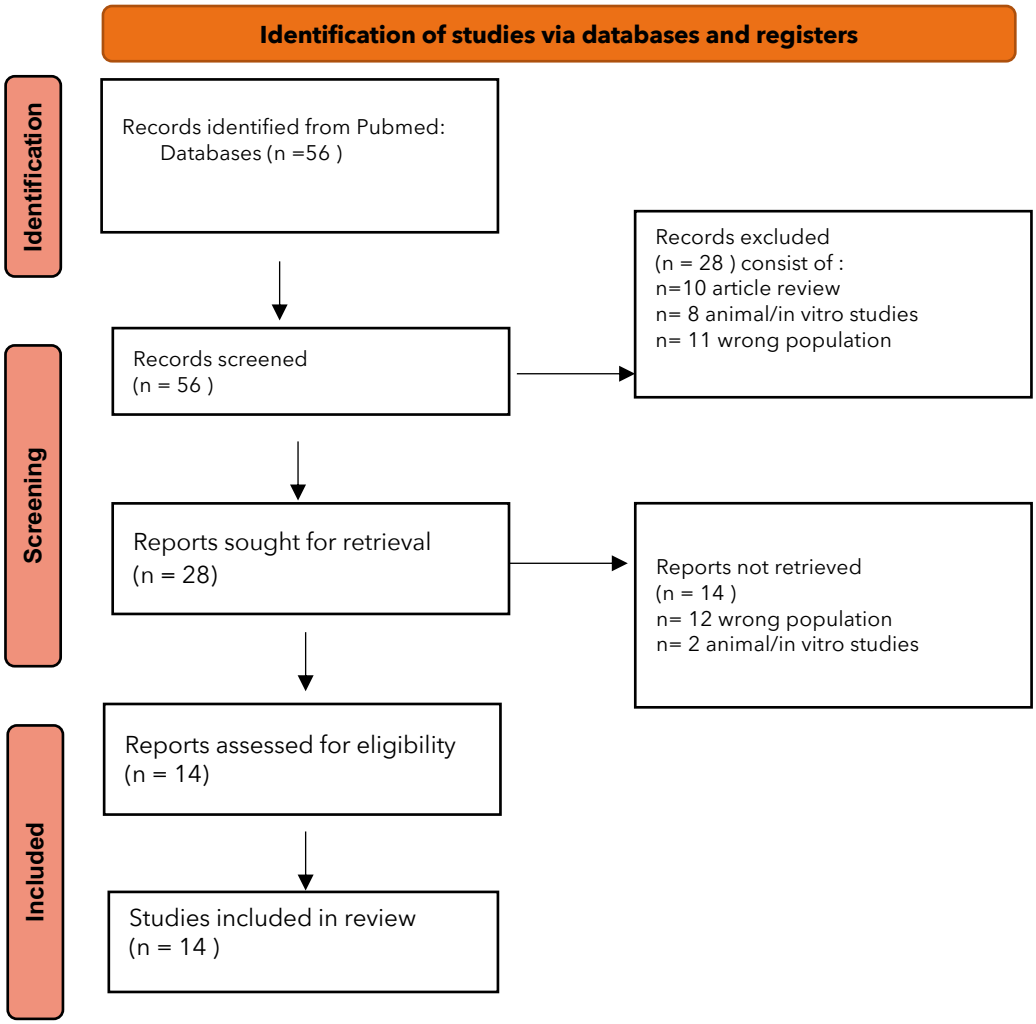

Figure 1. PRISMA flow diagram

Instrument and Procedures

Utilizing a systematic literature review method, this study assessed the prevalence, clinical relevance, and significance of drug transporter polymorphisms in the Indonesian population. A structured process was employed to ensure the reliability and validity of data extraction and analysis. In conclusion, this study utilized a multi-step research process, starting with identifying relevant studies, extracting data, and assessing quality, followed by synthesis of results to identify patterns and gaps within the field. Twelve studies that fell under the inclusion criteria were selected, and information pertaining to sample size, study design, genetic variants, pharmacokinetic and pharmacodynamic outcomes, and therapeutic implications were obtained from each of the studies using a standardized data extraction framework. The methodological quality of each study was assessed critically, including statistical robustness, population representability, and clinical applicability. Studies were also assessed for comparable common findings, inconsistencies and potentially confounding factors to ensure internal and external validity and findings. Studies that colonized the data of SLC22A1, SLCO1B1, and ABCB1 polymorphisms were discussed in this paper since these transporters have an essential role in the variability of drug response in Indonesia. Results were synthesized to note wide trends, gaps in knowledge and future areas for research. This group was appraised using rigorous methodology, allowing the assessment of the nascent field of pharmacogenetics in Indonesia to guide future studies toward personalized medicine and clinically informative outcomes for the country.

Data Analysis

Using a qualitative synthesis approach, thematic coding and comparative analysis of drug transporter polymorphisms were performed on 14 studies that included the Indonesian population. Extracted variables included sample size, genetic variants, population demographic information, study design, and clinical relevance. SLC22A1, SLCO1B1, and ABCB1 were chosen as targets based on their crucial involvement in drug transport and their relevance to drugs frequently prescribed in Indonesia. Polymorphisms in the SLC22A1 (OCT1) gene likely influence metformin uptake and glycemic control in patients with type 2 diabetes. Variants of the SLCO1B1 c.521T>C have been associated with statin-induced myopathy, which is essential since Indonesia has one of the highest prevalences

of hypercholesterolemia. Polymorphisms within the ABCB1 (MDR1) gene, like C3435T and G2677T, have been implicated in drug resistance in epileptic patients as well as the outcome of chemotherapy. However, their distribution and clinical consequences in Indonesians have yet to be explored in-depth. The challenges identified include small sample sizes, high research costs, and limited access to genetic screening. The study on SLC22A1 polymorphisms in diabetic patients included only 80 subjects, which limits the statistical power for genotype-phenotype correlation. As with most research on ABCB1 polymorphisms in patients undergoing chemotherapy, there were several challenges associated with the process of genetic testing due to the relatively high costs and limited infrastructure. These hurdles point towards greater research funding needs, more standardized pharmacogenetic guidelines, and better access to genetic testing. From integrating this knowledge, this study aspires to become a basis of pharmacogenetics advancement in Indonesia to improve drug safety, drug efficacy, and personalized medicine implementation.

Research Results

Following an extensive review of the existing literature pertaining to polymorphisms of drug transporters within the Indonesian demographic, a total of 14 relevant studies were discerned. These scholarly investigations examined a range of transporters implicated in the metabolism of various pharmacological agents, encompassing, but not limited to, oncology therapeutics (cyclophosphamide, Imatinib, anthracyclines), hypoglycemic medications (metformin), anticonvulsants (carbamazepine), lipid-lowering agents (simvastatin), Antiplatelet (clopidogrel) and treatments for tuberculosis. An organized summary of these investigations is presented below for further consideration:

Table 1. Drug Transporters Polymorphisms Among Indonesian Population Studies

Related Therapeutical Agents	Related Drug Transporter Polimorphisms	Key Findings	References
Cancer			
Cyclophosphamid	GTSP1A313G	60.4% wildtype (A/A); 29.7% heterozygous (A/G); 9.9% homozygous mutant (G/G). The G allele (A/G & G/G) is correlated with significantly more severe leukopenia compared with those bearing the wild-type allele (A/A) ($p<0.05$)	[22]
Imatinib	ABCB1 C1236T	The frequencies of the SNPs were CC (40%), CT (46%), and TT (14%). This finding reveals no association between polymorphism of *ABCB1* C1236T and imatinib response in Indonesian patients, with OR = 0.646 (95% CI: 0.283, 1.471; $p>0.05$	[**Error! Reference source not found.**]
Antracyclin	ABCB1, C1236T, C3435T, G2677T	The study noted a decrease in absolute neutrophil count (ANC) and an increase in levels of anemia during cycles of chemotherapy (Mean ± SD: 5,644.4 ± 2,962.5 mm3 vs. 3,034.8 ± 2,049.6 mm3; 12.1 ± 1.5 g/dL vs. 11.2 ± 1.3 g/dL) ($p< 0.050$). There was no association between GSTP1 polymorphisms and the rates of anemia and neutropenia ($p<0.050$). In addition, no ascertainable deviation from Hardy-Weinberg Equilibrium (HWE) was observed for the distribution of ABCB1 and GSTP1 genotypes and alleles ($p<0.050$).	[24]
NA	OCT1 (SNP from OCT 1; rs12208357, rs55918055, rs34130495, rs34059508)	The findings depicted that no varieties of genetic mutations were found for the 4 SNPs studied in the 202 Indonesian populations with cancer. The Met420del variant was identified in only 1.5% of the patients. This finding is consistent with earlier studies done in Japanese and Chinese cohorts.	[**Error! Reference source not found.**]
Tuberculosis			
TB Therapy	ABCB1 rs1128503 and rs1045642	The ABCB1 alleles rs1128503 and rs1045642 displayed heterogeneous genetic backgrounds (CC, CT and TT), while that of CYP2E1 rs3813867 was only CC (wild type). No significant association with duration of tuberculosis therapy was observed in the individual genetic variations in ABCB1 and CYP2E1. However, results of this study could provide insight of ABCB1 (rs1128503 and rs1045642) and CYP2E1 (rs3813867) in Indonesian population.	[26]

TB Therapy	SLCO1B1	Polymorphism c.463C>A (rs11045819) was absent, while heterozygous and homozygous polymorphisms of c.85-7793C>T (rs4149032) were present in 74 (51.0%) and 56 (38.6%) patients, respectively. For c.85-7793C>T (rs4149032), the minor allele frequency (MAF) for the T (mutant) allele was found to be 64.13% (186/209), which was greater than that found in the general population (MAF for rs4149032, 53.6%) reported in the 1000 Genomes. The frequency of SLCO1B1*15 haplotype was 63.9%.	[27]
Rifampin	SLCO1B1 SLCO1B3	Association between the SNPs of the SLCO1B1 gene and clinical outcome was also observed, where the SLCO1B1*15 haplotype was linked to susceptibility to failure of clinical outcome (p=0.005; RR=4.52; 95% CI: 1.22-16.64). The OATP1B1*15 haplotype showed a significantly higher risk for failure of clinical outcome than the three other haplotypes.	[**Error! Reference source not found.**]
Diabetes Mellitus			
Metformin	SLC22A1 Met420del	SLC22A1 Met420del gene did not encounter any AA variant (wild type) type, only 4% of subjects had Aa heterozygote type. The allele frequencies of A and a in all subjects were 2.0% and 98.0%, respectively.	[27]
	SLCO1B1	Polymorphism of c.463C>A(rs11045819) was not found and heterozygous and homozygous polymorphism of c.85-7793C>T(rs4149032) were discovered in 74 (51.0%) and 56 (38.6%) patients, respectively. The minor-allele frequency (MAF) of T (mutant) allele of c.85-7793C>T(rs4149032) is 64.13% (186/209), which was higher than in general population, the MAF of which the rs4149032 is 53.6% based on 1000 genome database.	[**Error! Reference source not found.**]
	OCT1, especially rs628031, rs122083571, and rs623442	The minor allele frequency (MAF) for the rs628031 polymorphism within this population was 0.59, with genotype frequencies for AA, AG, and GG accounting for 16.5%, 48.9%, and 34.6% respectively. The MAF for the rs623442 polymorphism was 0.20, with genotype frequencies of 5.4% CC, 29.0% CA and 65.6% AA. This population did not contain the rs122083571 polymorphism with 100% genotype CC. In this population, the genetic polymorphism of OCT1 rs628031 showed relatively high prevalence, while polymorphism of OCT1 rs623442 was present in only one-fifth of the studied population.	[**Error! Reference source not found.**]
Epilepsy			
Carbamazepine	ABCB1C3435T	The frequencies of subjects with C allele in ABCB1 C3435T gene were 53%, which was higher than that of T allele.	[**Error! Reference source not found.**]
Carbamazepine	MDR1 C3435T	Genotype do not distribute equally among groups in a study with 86 cases (61 in the study group and 25 in the control group) (0.58 vs. 0.42, p = 0.000, chi-square = 0.54). The concentrations of therapeutic doses of carbamazepine (dCBZ) in the study group were consistently higher than the therapeutic plasma levels (plCBZ) across all genotypes. In 37 subjects, criteria were met for drug-resistant epilepsy (DRE). The distribution of C and T was 0.63 vs. 0.37 (chi-square = 10.4) and 0.55 vs. 0.45 (chi-square = 6.17, p = 0.019) in DRV and DRE, respectively. Tukey's multiple comparison post hoc test showed that, in DRV, CT genotype had significantly lower dCBZ (330.36 ± 174.91 mg) and plCBZ (7.15 ± 2.64 mcg/mL) than all genotypes in DRE. Despite an average dCBZ dose of ~800 mg, plCBZ levels exceeded the toxic level with the highest levels detected in TT individuals.	[**Error! Reference source not found.**]
Cholesterol			
Simvastatin	SLC01B1, SNP c.521T>C	In a study, which consisted of a total of 71 hypercholesterolemia patients, the SNP c.521T>C was present in 9.9% of patients. Chi-square analysis revealed	[**Error! Reference source not found.**]

		no significant association between the SNP c.521T>C (TC genotype) and flow-mediated dilation (FMD) (p = 0.973). However, logistic regression analysis showed that use duration of simvastatin medication was associated with an increased incidence (Adjusted Odds Ratio [Adj. OR] = 2.424; Confidence Interval [CI] = 1.117-5.260, p = 0.025) and a decrease in systolic blood pressure (Adj. OR = 0.92; CI = 0.025–0.333, p = 0.001	
Stroke			
Clopidogrel	ABCB1 C1236T	ABCB1 C1236T homozygote wildtype linked to higher bleeding risk. 12.9% of subjects were non-responsive to clopidogrel. Genotype frequencies: C3435T (35.9% CC, 43.5% CT, 16.9% TT). Genotype frequencies: C1236T (17.8% CC, 39.5% CT, 42.7% TT). No significant association found for C3435T and clopidogrel responsiveness. Monitoring for bleeding risk is essential in clopidogrel use.	[**Error! Reference source not found.**]

Population Representation in Included Studies

Population and ethnic representation were not consistently reported across the 14 studies reviewed. Out of the abovementioned studies, seven studies specified the ethnic background of participants; four studies involved Javanese populations, one study involved Balinese participants, one study involved Sundanese participants and one mixed multi-ethnic sample study from North Sumatra consisting of Bataknese, Acehnese, Malay, and Chinese-Indonesian (Tionghoa) individuals. The remaining studies did not report specific identities, although the studies' locations (Jakarta, Yogyakarta, Surabaya and Samarinda) allow for limited inference. Most studies were focused on western and central Indonesia, namely Java, Sumatra, and Bali. There was only one study from Kalimantan (Samarinda, East Kalimantan), and no ethnic demographics were reported. None of the studies included participants from Eastern Indonesia, including Sulawesi, Nusa Tenggara, Maluku or Papua—regions that are genetically diverse and are under study in biomedical research. Such geographical and ethnic concentration may not be representative of the current findings and may prevent the implementation of pharmacogenetic findings from being equitably implemented in the heterogeneous Indonesian population. Studies that can be designed and published to engage individuals from minority ethnicities and global areas will enhance the diversity of future pharmacogenetic research and its relevance to individual diversity. This is critical to the development of personalized medicine that is scientifically sound and socially equitable. Ethnic and geographic representation is summarized in Table 2.

Table 1. Population and Ethnic Representation in Included Studies

No	Author (year)	Study Location	Reported or Inferred Ethnic Group	Total Participants
1	Hasni et al. (2016) [22]	Medan (North Sumatera)	Bataknese (45.1%), Javanese (33.3%), Acehnese (9.9%), Malay (8.8%), others (3.3%)	91
2	Rinaldi et al. (2019) [**Error! Reference source not found.**]	Jakarta	Not reported	120
3	Syarifah et al. (2022) [24]	Medan (North Sumatera)	Bataknese (49.3%), Javanese (32.6%), Acehnese (11.6%), Tionghoa (0.7%), Malay (3.6%), Minangkabau (2.2%)	138
4	Perwitasari et al. (2014) [**Error! Reference source not found.**]	Yogyakarta	Not reported	202

5	Barliana et al. (2021) [26]	Jambi (Central Sumatera)	Not reported	50
6	Santoso et al. (2022) [27]	Bandung (West Java)	Sundanese (92.4%), Javanese (4.8%), Ambonese/South Moluccans (0.7%), Bataknese (0.7%), Buginese (0.7%), Minangnese (0.7%)	145
7	Ang et al. (2018) [**Error! Reference source not found.**]	Samarinda (East Kalimantan)	Not reported	36
8	Ningrum et al. (2019) [27]	Yogyakarta	Javanese	100
9	Ningrum et al. (2018) [**Error! Reference source not found.**]	Yogyakarta	Javanese	86
10	Aryastuti et al. (2022) [**Error! Reference source not found.**]	Bali	Balinese	133
11	Istikharah et al. (2020) [**Error! Reference source not found.**]	Yogyakarta	Javanese	100
12	Budikayanti et al. (2023) [**Error! Reference source not found.**]	Jakarta	Not reported	86
13	Andrianto et al. 2022 [**Error! Reference source not found.**]	Surabaya (East Java)	Not reported	71
14	Hidayat et al. 2024 [**Error! Reference source not found.**]	Jakarta	Not reported	124

Discussion

Genetic variation in drug transporters has emerged as a key determinant of interindividual variability in drug disposition and, consequently, drug action and toxicity. This study aimed to explore polymorphisms in clinically relevant drug transporters, including ABCG2, SLCO1B1, and SLC22A1, based on their possible roles in the genetically heterogeneous Indonesian population. These questions need to be answered to optimize pharmacotherapy in Indonesia by implementing personalized medicine.

For the first research question, the top three most published drug transporter polymorphisms within the Indonesian population are as follows: SLCO1B1 (rs4149056), SLC22A1 (Met420del, rs628031), and ABCB1 (rs1045642, rs2032582). These have mostly been studied in Javanese, Sundanese, Balinese, and Bataknese. Out of

14 studies included, 5 reports were related to ABCB1, 3 to SLCO1B1, and others to OCT1, SLC22A1, and GTSP, confirming their local relevance. One caveat to this is that these findings may still underestimate the actual diversity of transporter polymorphisms in Indonesia due to the limited geographical sampling and relatively small cohort sizes.

Polymorphisms affect drug pharmacokinetics and pharmacodynamics by modifying absorption, distribution, metabolism, and excretion (question 2). SLCO1B1 polymorphisms, for example, lessen the hepatic uptake of statins and increase systemic concentrations and the risk of side effects [36–42]. Variants of SLC22A1 mediate hepatocyte transport of metformin and thus mediate its glucose-lowering efficacy [43-50]. Variants of ABCB1 have been associated with differential responses to cancer chemotherapy and antiemetics [18,19,23,24,33]. These findings are in line with studies from other regions, such as Africa, describing ethnicity-related transporter effects [51,52]. However, notwithstanding all overlaps, there are still genotype-drug response relationships that are population-specific , highlighting the role of local research.

In terms of the 3rd research question, associations between transporter polymorphisms and clinical responses or adverse events have been evident from previous work. As an example, variants in SLCO1B1, an OAT3 variant, are associated with statin-induced myopathy [39,40], ABCB1 polymorphisms with clopidogrel resistance [35] and chemotherapy-induced nausea [18]. Observational studies have shown that SLC22A1 polymorphisms exert differential effects on metformin pharmacokinetics and glycemic response based on allele type and patient phenotype [43–50]. Nonetheless, variation between the findings of some studies may be due to a small sample size, a lack of ethnic diversity, or differences in study design. Further clinical studies, ideally designed in a prospective manner and associated with pharmacodynamic outcomes are required to validate these relationships in the Indonesian setting.

Several key challenges related to infrastructure (e.g., no national pharmacogenomic databases), underfunded research, and a lack of awareness among clinicians hamper the integration of pharmacogenetics in Indonesia, answering the fourth research question [15,16]. Also, the differences between international guidelines and local clinical practice worsen things [17]. The solutions consist of investment in next-generation sequencing [13], education of healthcare workers, supportive policy, and building specific guidelines for the population. International collaborations with consortia like the Pharmacogenomics Global Research Network [2] may also accelerate implementation via knowledge and resource sharing.

Concerning the fifth research question, Indonesia's impressive genetic diversity is both an opportunity and a challenge. Although it allows very precise pharmacogenetic strategies, population-based studies have shown significant underrepresentation from Sulawesi, Maluku, Nusa Tenggara, and Papua in research to date. As xenobiotic transporters display ethnic specificity in pharmacogenomic studies, country-wide genotype-specific recommendations must be validated using regionally representative sampling. Public databases like PharmFreq [14] provide a good starting point but require local efforts to ensure their contention.

Our study revealed that the most important transporter polymorphisms were ABCG2 rs2231142, SLCO1B1 rs4149056, and SLC22A1 Met420del [53]. These achieve genome-wide significance thresholds and replicated associations with drug response. Polymorphisms in SLCO1B1 and ABCG2 have been associated with altered responses to statins {34,36-42], allopurinol [54,55], methotrexate [56-58] and cardiovascular agents [34,35], and SLC22A1 variants affect metformin [43-50], sumatriptan and others [59-61]. In vitro and clinical studies confirm the functional significance, with decreased transporter activity and expression associated with altered systemic drug concentrations.

From a clinical perspective, these polymorphisms matter in treating diseases common in Indonesia, such as tuberculosis, cancer, diabetes, and cardiovascular disease. Because drugs such as rifampicin, metformin, statins, and chemotherapeutics are widely used and transporters are known to modulate the pharmacokinetics of these drugs, transporter genotyping may guide safer and more effective treatment strategies. Ongoing research demonstrates that transporter genotypes can influence therapeutic drug response as well as toxicity risk. This genotype was shown to be associated with imatinib resistance in chronic myeloid leukemia and altered carbamazepine levels in epileptic patients [23,33].

Unexpected variability in the extent of clinical association, most notably in SLC22A1 and metformin studies, also exists. The variability in clinical outcomes is likely due to differences in genotype frequency, environmental factors, including dietary factors and other broader exposure, such as to pesticides [10], or modulation by transcriptional factors, including PXR and CAR [3,12]. In addition, epigenetic mechanisms or inflammation may also result in inter-individual variation of transporter expression at the cellular level, ultimately complicating genotype-phenotype correlations [4,5]. These layers of complexity further highlight the importance of taking a holistic approach that incorporates genetic, environmental, and physiological factors in personalized medicine.

Probably the most outstanding limitation is the underrepresentation of eastern Indonesian ethnic groups. Most studies focus on Java, Sumatra or Bali, with very few on Sulawesi, Maluku, Nusa Tenggara or Papua. This limits the relevance of current pharmacogenetic findings [27]. Other challenges are the limited availability of molecular diagnostic tools, inconsistency in clinical documentation, and impeding genotype-phenotype outcome datasets. Overcoming these obstacles will necessitate systemic enhancements to data infrastructure, research funding, and regulatory frameworks.

This review is brazenly beneficial for science, as it endeavors to mend the jumbled data about transporter polymorphisms into a single gist yet bred a framework that is unique to Indonesia. Our work synthesizes disparate results into a unified framework for the application of precision medicine. Our identification of transporter genes meeting international validation criteria [53] is of scientific novelty; it provides evidence for the prioritization of transporter genes in local research and practice [53]. In addition, this work contextualizes findings across the Indonesian healthcare landscape and provides strategic priorities to ensure the equitable application of findings.

Future pharmacogenetic studies in Indonesia should include strategies of inclusive samples in addition to economic evaluation to determine feasibility. A national database summarizing transporter allele frequencies and their clinical implications would be of tremendous help to clinicians and researchers making evidence-based decisions. The integration with electronic medical records and the generation of clinical decision support tools would further facilitate the application of pharmacogenetics in daily practice.

These transporter polymorphisms should be an excellent approximation for explaining the interindividual variability with respect to drug response in Indonesia, particularly ABCG2, SLCO1B1, and SLC22A1 polymorphisms. Filling gaps in infrastructure, continuing to support equitable research, and coordinating the integration of pharmacogenetics into clinical workflows will ensure equitable access to personalized medicine nationwide. Genomic advances will, however, need to be translated into health improvements, and that will require collaboration between researchers, clinicians, policy-makers and the wider public that funds this work.

Conclusions and Implications

This review serves as an additional reminder of the significant impact of drug transporter polymorphisms in terms of pharmacokinetics, pharmacodynamics, and clinical treatment outcomes. Pharmacogenetics's introduction into Indonesia's health care system is vital in advancing personalized medicine, improving therapeutic efficacy and safety. However, as current studies are predominantly based in Java, Sumatra, Bali, and parts of Kalimantan, there are limits to their applicability to populations at large. For fair pharmacogenomic implementation, we need more inclusion from underrepresented territories, particularly Eastern Indonesia. We propose creating a national pharmacogenetic policy framework to aid this integration, including supportive genetics research funding, clinical guideline creation, workforce development, and public engagement initiatives. These efforts will enhance evidence-based, equitable and sustainable personalized healthcare across Indonesia.

Limitation

Several limitations may restrict the scope and applicability of its findings, which this review recognizes. First, the literature search was restricted to the PubMed database and English-language articles, which may have missed relevant studies published in other languages or indexed in local and regional databases. Another factor is the small sample size of many of these studies, reducing the statistical power to detect robust associations and the external validity of the results. Third, the heterogeneity of methods across studies (e.g., differences in study design, genotyping techniques and outcome measures) made it difficult to synthesize consistent conclusions. Finally, the geographic and ethnic diversity of the study populations is limited and would not fully capture Indonesia's genetic diversity landscape. These limitations emphasize the necessity of conducting future large-scale, multi-center studies encompassing diverse populations, standardized methodologies, and a wider range of data sources to reinforce the evidence base for pharmacogenetics and facilitate its incorporation into personalized healthcare strategies in Indonesia.

Suggestion for Future Research

Future Indonesian pharmacogenetic studies during 2025–2030 should focus on several already recognized priorities. First, there is an urgent need for population-based studies mapping the distribution of key transporter gene polymorphisms, such as SLCO1B1, SLC22A1, ABCB1, and ABCG2, in diverse ethnic groups, especially in underrepresented regions such as Sulawesi, Maluku, Nusa Tenggara and Papua. Clinical validity over the impact of these polymorphisms on drug response and adverse effects needs to be established in the implementation of popular drugs used in Indonesia, e.g., statins, metformins, tamoxifen and anti-tuberculosis drugs. Third, the research should facilitate developing and validating genotype-guided dosing algorithm models, particularly for narrow

therapeutic indices such as warfarin or phenytoin, to ascertain their feasibility in Indonesian clinical scenarios. Furthermore, establishing a national pharmacogenomic database summarizing frequencies of variants and their associated clinical outcomes would serve as a useful reference point for practicing physicians and research scientists. It will also be critical to strengthen local capacity by introducing advanced technologies like next-generation sequencing and investing in the education and training of health professionals. By working hand-in-hand, such focused efforts will facilitate the implementation of pharmacogenetics into the Indonesian healthcare system and enable the distribution of personalized medicine across the country in an evidence-based manner.

Declarations

Author Contributions

Conceptualization, Ida Adhayanti and Abdul Gafur; methodology, Ida Adhayanti ; software, Ida Adhayanti.; validation, Ida Adhayanti and Abdul Gafur.; formal analysis, Ida Adhayanti.; investigation, Ida Adhayanti.; resources, Ida Adhayanti and Abdul Gafur; data curation, Abdul Gafur; writing–original draft preparation, Ida Adhayanti and Abdul Gafur.; writing–review and editing, Ida Adhayanti and Abdul Gafur.; visualization, Ida Adhayanti and Abdul Gafur.; supervision, Ida Adhayanti and Abdul Gafur.; project administration, Ida Adhayanti and Abdul Gafur.

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Conflicts of Interest

The authors declares that there is no conflict of interests regarding the publication of this manuscript.

References

1. Simanjuntak R, Sutrisman H, Prihartanto A, Ramadhona R. Pharmacogenomic analysis in determining optimal drug dosage in chronic disease patients in Indonesia. Int J Public Health. 2024;1(3). https://doi.org/10.62951/ijph.v1i3.74
2. Cavallari LH, Hicks JK, Patel JN, Elchynski AL, Smith DM, Bargal SA, et al. The Pharmacogenomics Global Research Network Implementation Working Group: global collaboration to advance pharmacogenetic implementation. Pharmacogenet Genomics. 2024. https://doi.org/10.1097/fpc.0000000000000547
3. Koo SH, Lo YL, Yee JY, Lee EJD. Genetic and/or non-genetic causes for inter-individual and inter-cellular variability in transporter protein expression: implications for understanding drug efficacy and toxicity. Expert Opin Drug Metab Toxicol. 2015;11(12):1933–45. https://doi.org/10.1517/17425255.2015.1104298
4. Chan SL, Jin S, Loh M, Brunham LR. Progress in understanding the genomic basis for adverse drug reactions: a comprehensive review and focus on the role of ethnicity. Pharmacogenomics. 2015;16(16):1905–26. https://doi.org/10.2217/pgs.15.54

5. Bachtiar M, Ooi BNS, Wang J, Jin Y, Tan TW, Chong SS, et al. Towards precision medicine: interrogating the human genome to identify drug pathways associated with potentially functional, population-differentiated polymorphisms. Pharmacogenomics J. 2019;19(5):419–28. https://doi.org/10.1038/s41397-019-0096-y

6. Atmaja SP, Rawar E, Kristiyani A, Nugrahaningsih DAA, Sadewa AH, Patramurti C. The genetic polymorphisms of CYP3A4*1G and CYP3A5*3 in Javanese Indonesian population. J Trop Life Sci. 2024;14(1):51–6. https://doi.org/10.11594/jtls.14.01.06

7. Santoso P, Juliastuti H, Nataprawira HM, Soeroto AY, Alisjahbana B, Ruslami R, Debora J, Sribudiani Y, Maskoen AM. Polymorphisms of SLCO1B1 Gene in Sundanese Ethnic Population of Tuberculosis Patients in Indonesia. Acta Med Indones. 2022 Oct;54(4):517-523. PMID: 36624704.

8. Hidayat R, Rasyid A, Harris S, Harahap A, Herqutanto H, Louisa M, et al. Impact of Cyp2c19 Allele 17 Mutase on Clopidogrel Hyper-Responsiveness in Indonesian Patients with Ischemic Stroke. Open Access Maced J Med Sci. 2023;11(G):367–74. https://doi.org/10.3889/oamjms.2023.11558

9. Alvina AP, Zullies I, Sri S, Anindya R. High Frequency of the Opioid Receptor μ-1 (OPRM1) A118G Polymorphism, an Opioid Drug Therapy Related Gene, in the Indonesian Population. Curr Pharmacogenomics Pers Med. 2020;18(3):213–9. https://doi.org/10.2174/1875692117666191211154755

10. Banerjee BD, Kumar R, Thamineni KL, Shah HK, Thakur GK, Sharma T. Effect of environmental exposure and pharmacogenomics on drug metabolism. Curr Drug Metab. 2020;21(1):3–11. https://doi.org/10.2174/1389200221666200110153304

11. Jamshidi N, Nigam SK. Drug transporters OAT1 and OAT3 have specific effects on multiple organs and gut microbiome as revealed by contextualized metabolic network reconstructions. Sci Rep. 2022;12:18242. https://doi.org/10.1038/s41598-022-21091-w

12. Liang X, Staiger KM, Riddle E, Hao J, Lai Y. Role of transporters in drug disposition and drug-drug interactions. In: Varma MV, El-Kattan A, editors. ADME-enabling technologies in drug design and development. 1st ed. San Diego (CA): Academic Press; 2020. p. 275–300. DOI: https://doi.org/10.1016/B978-0-12-820018-6.00010-7

13. Kothary AS, Mahendra C, Tan M, Tan EJM, Yi JPH, Gabriella G, et al. Validation of a multi-gene qPCR-based pharmacogenomics panel across major ethnic groups in Singapore and Indonesia. Pharmacogenomics. 2021;22(14):857–69. https://doi.org/10.2217/pgs-2021-0071

14. Tremmel R, Zhou Y, Camara MD, Laarif S, Eliasson E, Lauschke VM. PharmFreq: a comprehensive atlas of ethnogeographic allelic variation in clinically important pharmacogenes. Nucleic Acids Res. 2024;52(D1):D1181–9. https://doi.org/10.1093/nar/gkae1016

15. Ausi Y, Barliana MI, Postma MJ, Suwantika AA. One Step Ahead in Realizing Pharmacogenetics in Low- and Middle-Income Countries: What Should We Do? J Multidiscip Healthc. 2024;17:101–8. https://doi.org/10.2147/JMDH.S458564

16. Dizon JM, Machingaidze S, Grimmer K. To adopt, to adapt, or to contextualise? The big question in clinical practice guideline development. BMC Res Notes. 2016;9:442. https://doi.org/10.1186/s13104-016-2244-7

17. Widyahening IS, Wangge G, van der Graaf Y, van der Heijden GJMG. Adapting clinical guidelines in low-resources countries: a study on the guideline on the management and prevention of type 2 diabetes mellitus in Indonesia. J Eval Clin Pract. 2017;23(1):121–7. https://doi.org/10.1111/jep.12628

18. Perwitasari DA, Wessels JAM, van der Straaten RJHM, Baak-Pablo R, Mustofa M, Nortier JWR, et al. Association of ABCB1, 5-HT3B receptor and CYP2D6 genetic polymorphisms with ondansetron and metoclopramide antiemetic response in Indonesian cancer patients treated with highly emetogenic chemotherapy. Jpn J Clin Oncol. 2011;41(11):1302–9. https://doi.org/10.1093/jjco/hyr117

19. Kulma I, Boonprasert K, Na-Bangchang K. Polymorphisms of genes encoding drug transporters or cytochrome P450 enzymes and association with clinical response in cancer patients: a systematic review. Cancer Chemother Pharmacol. 2019;84(3):405–22. https://doi.org/10.1007/s00280-019-03932-0

20. Pasternak AL, Ward KM, Irwin M, Okerberg C, Hayes D, Fritsche LG, et al. Identifying the prevalence of clinically actionable drug-gene interactions in a health system biorepository to guide pharmacogenetics implementation services. Clin Transl Sci. 2022;15(5):1217–25. https://doi.org/10.1111/cts.13449

21. Maharani L, Yugatama A. Prevalence of adverse drug reaction in Indonesia: A systematic review. J Appl Pharm Sci [Internet]. 2023; Available from: http://dx.doi.org/10.7324/japs.2023.91550

22. Hasni D, Siregar KB, Lim H. The influence of glutathion S-transferase P-1 polymorphism A313G rs1695 on the susceptibility to cyclophosphamide hematologic toxicity in Indonesian patients. Medical Journal of Indonesia. 2016 Jul 26;25(2):118–26. https://doi.org/10.13181/mji.v25i2.1308

23. Rinaldi I, Nova R, Widyastuti R, Priambodo R, Instiaty I, Louisa M. Association between C1236T genetic variant of ABCB1 gene

and molecular response to imatinib in Indonesian chronic myeloid patients. *Asian Pac J Cancer Prev*. 2019;20(11):3331–4. https://doi.org/10.31557/APJCP.2019.20.11.3331

24. Syarifah S, Widyawati T, Hasni D, Sari MI, Rusdiana R, Hamdi T. The Relation of Haplotype ATP-binding Cassette B1 and Glutathione S-transferase P1 A313G Genes with Hematological Toxicity in Indonesian Breast Cancer Patients Receiving Chemotherapy. Oman Med J. 2022 Mar 22;37(2):e357. doi: 10.5001/omj.2022.36. PMID: 35402005; PMCID: PMC8976885.
25. Perwitasari DA, Attobari J. Polymorphism of organic cation transporter 1 (OCT1) in Indonesian cancer patients. Int J Pharm Pharm Sci. 2014;6(5):380–2.
26. Barliana MI, Kusuma ASW, Insani WN, Alfian SD, Diantini A, Mutakin M, et al. Genetic variation of ABCB1 (rs1128503, rs1045642) and CYP2E1 rs3813867 with the duration of tuberculosis therapy: a pilot study among tuberculosis patients in Indonesia. BMC Res Notes. 2021;14(1). https://doi.org/10.1186/s13104-021-05711-8
27. Ang SA, Nugroho AK, Sadewa AH, Hakim L, Mustofa. The SLCO1B1*15 haplotype associated with lower clinical outcome in Indonesian tuberculosis patients. Berkala Ilmu Kedokteran [Internet]. 2018;50(01):50–9. Available from: http://dx.doi.org/10.19106/jmedsci005001201806
28. Ningrum VD, Istikharah R, Firmansyah R. Allele frequency of SLC22A1 Met420del metformin main transporter encoding gene among Javanese-Indonesian population. Open Access Maced J Med Sci. 2019 Feb 14;7(3):378–83. doi:10.3889/oamjms.2019.087. PMID: 30834005; PMCID: PMC6390162.
29. Ningrum VDA, Ikawati Z, Sadewa AH, Ikhsan MR. Allele frequencies of two main metformin transporter genes: SLC22A1 rs628031 A>G and SLC47A1 rs2289669 G>A among the Javanese population in Indonesia. Curr Pharmacogenomics Person Med. 2018 Feb 21;15(2):121–8.
30. Aryastuti SA, Sintya E, Asri Lestarini AL, Witari NPD. Allele frequency of a common variant and two common loss-of-function variants in organic cation transporter 1 (OCT1) among Balinese diabetic patients. Biomed Pharmacol J. 2022 Mar 31;15(1):269–75. doi:10.13005/bpj/2363.
31. Istikharah R, Hartienah SD, Vitriyani S, Ningrum VDA. Allele frequency of carbamazepine major efflux transporter encoding gene ABCB1 C3435T among Javanese-Indonesian population. Open Access Maced J Med Sci. 2020 Jul 20;8(A):406–13. doi:10.3889/oamjms.2020.4184.
32. Budikayanti A, Khosama H, Octaviana F, Hamid DH, Louisa M, Ranakusuma TAS, Setiabudy R. Multidrug resistance-1 C3435T polymorphism and carbamazepine plasma level in Indonesian temporal lobe epilepsy patients. Curr Drug Saf. 2023;18(1):62–8. doi:10.2174/1574886317666220414130526. PMID: 35430998.
33. Andrianto, Puspitasari M, Ardiana M, Dewi IP, Shonafi KA, Kusuma Wardhani LF, Nugraha RA. Association between single nucleotide polymorphism SLCO1B1 gene and simvastatin pleiotropic effects measured through flow-mediated dilation endothelial function parameters. Ther Adv Cardiovasc Dis. 2022;16:17539447221132367. doi:10.1177/17539447221132367. PMID: 36314075.
34. Hidayat R, Nabilah RA, Fisher M, Aninditha T, Kurniawan M, Estiasari R, et al. The association between ABCB1 gene polymorphism and clopidogrel response variability in ischemic stroke: a cross-sectional study. BMC Neurol. 2024 Jun 24;24(1):216. doi:10.1186/s12883-024-03723-y. PMID: 38914966; PMCID: PMC11194867.
35. Chasman DI, Giulianini F, MacFadyen J, Barratt BJ, Nyberg F, Ridker PM. Genetic determinants of statin-induced low-density lipoprotein cholesterol reduction. Circ Cardiovasc Genet. 2012 Apr;5(2):257–64. doi:10.1161/CIRCGENETICS.111.961144.
36. Bailey KM, Romaine SPR, Jackson BM, Farrin AJ, Efthymiou M, Barth JH, et al. Hepatic metabolism and transporter gene variants enhance response to rosuvastatin in patients with acute myocardial infarction. Circ Cardiovasc Genet. 2010 Jun;3(3):276–85. doi:10.1161/CIRCGENETICS.109.898502.
37. Chu AY, Giulianini F, Grallert H, Dupuis J, Ballantyne CM, Barratt BJ, et al. Genome-wide association study evaluating lipoprotein-associated phospholipase A2 mass and activity at baseline and after rosuvastatin therapy. Circ Cardiovasc Genet. 2012 Dec;5(6):676–85. doi:10.1161/CIRCGENETICS.112.963314.
38. SEARCH Collaborative Group, Link E, Parish S, Armitage J, Bowman L, Heath S, et al. SLCO1B1 variants and statin-induced myopathy: a genomewide study. N Engl J Med. 2008 Aug 21;359(8):789–99. doi:10.1056/NEJMoa0801936. PMID: 18650507.
39. Voora D, Shah SH, Spasojevic I, Ali S, Reed CR, Salisbury BA, Ginsburg GS. The SLCO1B1*5 genetic variant is associated with statin-induced side effects. J Am Coll Cardiol. 2009 Oct 20;54(17):1609–16. doi: 10.1016/j.jacc.2009.04.053. PMID: 19833260; PMCID: PMC3417133.
40. Postmus I, Trompet S, Deshmukh HA, Barnes MR, Li X, Warren HR, et al. Pharmacogenetic meta-analysis of genome-wide association studies of LDL cholesterol response to statins. Nat Commun. 2014 Oct 28;5:5068. doi: 10.1038/ncomms6068.
41. Akao H, Polisecki E, Kajinami K, Trompet S, Robertson M, Ford I, et al. Genetic variation at the SLCO1B1 gene locus and low density lipoprotein cholesterol lowering response to pravastatin in the elderly. Atherosclerosis. 2012 Feb;220(2):413–7. doi: 10.1016/j.atherosclerosis.2011.09.028.

42. Shu Y, Brown C, Castro R, Shi R, Lin E, Owen R, et al. Effect of genetic variation in the organic cation transporter 1, OCT1, on metformin pharmacokinetics. Clin Pharmacol Ther. 2008 Feb;83(2):273–80. doi: 10.1172/JCI30558.

43. Sundelin E, Gormsen L, Jensen J, Vendelbo M, Jakobsen S, Munk O, et al. Genetic polymorphisms in organic cation transporter 1 attenuate hepatic metformin exposure in humans. Clin Pharmacol Ther. 2017 Nov;102(5):841–8. doi: 10.1002/cpt.701.

44. Tzvetkov MV, Saadatmand AR, Bokelmann K, Meineke I, Kaiser R, Brockmöller J. Effects of OCT1 polymorphisms on the cellular uptake, plasma concentrations and efficacy of the 5-HT3 antagonists tropisetron and ondansetron. Pharmacogenomics J. 2012 Feb;12(1):22–9. doi: 10.1038/tpj.2010.75.

45. Christensen MMH, Højlund K, Hother-Nielsen O, Stage TB, Damkier P, Beck-Nielsen H, et al. Endogenous glucose production increases in response to metformin treatment in the glycogen-depleted state in humans: a randomised trial. Diabetologia. 2015 Nov;58(11):2494–502. doi: 10.1007/s00125-015-3733-2.

46. Dujic T, Zhou K, Yee S, van Leeuwen N, de Keyser C, Javorský M, et al. Variants in pharmacokinetic transporters and glycemic response to metformin: a MetGen meta-analysis. Clin Pharmacol Ther. 2017 Jun;101(6):763–72. doi: 10.1002/cpt.567.

47. Jablonski KA, McAteer JB, de Bakker PIW, Franks PW, Pollin TI, Hanson RL, et al. Common variants in 40 genes assessed for diabetes incidence and response to metformin and lifestyle intervention in the Diabetes Prevention Program. Diabetes. 2010 Oct 1;59(10):2672–81. https://doi.org/10.2337/db10-0543

48. Zhou K, Donnelly LA, Kimber CH, Donnan PT, Doney ASF, Leese G, et al. Reduced-function SLC22A1 polymorphisms encoding organic cation transporter 1 and glycemic response to metformin: a GoDARTS study. Diabetes. 2009 Jun 1;58(6):1434–9. https://doi.org/10.2337/db08-0896

49. Christensen MMH, Brasch-Andersen C, Green H, Nielsen F, Damkier P, Beck-Nielsen H, et al. The pharmacogenetics of metformin and its impact on plasma metformin steady-state levels and glycosylated hemoglobin A1c. Pharmacogenet Genomics. 2011 Dec;21(12):837–50. https://doi.org/10.1097/FPC.0b013e32834c0010

50. Rajman I, Knapp L, Hanna I. Genetic diversity in drug transporters: impact in African populations. Clin Transl Sci. 2020 Sep;13(5):848–60. https://doi.org/10.1111/cts.12769

51. Hennig S, Naiker S, Reddy T, Egan D, Kellerman T, Wiesner L, et al. Effect of SLCO1B1 polymorphisms on rifabutin pharmacokinetics in African HIV-infected patients with tuberculosis. Antimicrob Agents Chemother. 2015 Oct 19;60(1):617–20. https://doi.org/10.1128/AAC.01195-15

52. Pritchard D, Patel JN, Stephens LE, McLeod HL. Comparison of FDA table of pharmacogenetic associations and Clinical Pharmacogenetics Implementation Consortium guidelines. Am J Health Syst Pharm. 2022 Jun 7;79(12):993–1005. https://doi.org/10.1093/ajhp/zxac064

53. Wen C, Yee S, Liang X, Hoffmann T, Kvale M, Banda Y, et al. Genome-wide association study identifies ABCG2 (BCRP) as an allopurinol transporter and a determinant of drug response. Clin Pharmacol Ther. 2015 May;97(5):518–25. https://doi.org/10.1002/cpt.89

54. Roberts RL, Wallace MC, Phipps-Green AJ, Topless R, Drake JM, Tan P, et al. ABCG2 loss-of-function polymorphism predicts poor response to allopurinol in patients with gout. Pharmacogenomics J. 2017 Mar;17(2):201–3. https://doi.org/10.1038/tpj.2015.101

55. Radtke S, Zolk O, Renner B, Paulides M, Zimmermann M, Möricke A, et al. Germline genetic variations in methotrexate candidate genes are associated with pharmacokinetics, toxicity, and outcome in childhood acute lymphoblastic leukemia. Blood. 2013 Jun 27;121(26):5145–53. https://doi.org/10.1182/blood-2013-01-480335

56. Ramsey LB, Panetta JC, Smith C, Yang W, Fan Y, Winick NJ, et al. Genome-wide study of methotrexate clearance replicates SLCO1B1. Blood. 2013 Feb 7;121(6):898–904. https://doi.org/10.1182/blood-2012-08-452839

57. Treviño LR, Shimasaki N, Yang W, Panetta JC, Cheng C, Pei D, et al. Germline genetic variation in an organic anion transporter polypeptide associated with methotrexate pharmacokinetics and clinical effects. J Clin Oncol. 2009 Dec 10;27(35):5972–8. https://doi.org/10.1200/JCO.2008.20.4156

58. Matthaei J, Kuron D, Faltraco F, Knoch T, Dos Santos Pereira J, Abu Abed M, et al. OCT1 mediates hepatic uptake of sumatriptan and loss-of-function OCT1 polymorphisms affect sumatriptan pharmacokinetics. Clin Pharmacol Ther. 2016 Jun 12;99(6):633–41. https://doi.org/10.1002/cpt.317

59. Tzvetkov MV, Matthaei J, Pojar S, Faltraco F, Vogler S, Prukop T, et al. Increased systemic exposure and stronger cardiovascular and metabolic adverse reactions to fenoterol in individuals with heritable OCT1 deficiency. Clin Pharmacol Ther. 2018 May 8;103(5):868–78. https://doi.org/10.1002/cpt.812

60. Giacomini KM, Balimane PV, Cho SK, Eadon M, Edeki T, Hillgren KM, et al. International Transporter Consortium commentary on clinically important transporter polymorphisms. Clin Pharmacol Ther. 2013 Jul;94(1):23–6. https://doi.org/10.1038/clpt.2013.12

61. Tsamandouras N, Dickinson G, Guo Y, Hall S, Rostami-Hodjegan A, Galetin A, et al. Development and application of a mechanistic pharmacokinetic model for simvastatin and its active metabolite simvastatin acid using an integrated population PBPK approach. Pharm Res. 2015 Jun 2;32(6):1864–83. https://doi.org/10.1007/s11095-014-1581-2