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Pharmacogenomics of Adverse Drug Reactions: Integrating Genetic Biomarkers into Precision Pharmacotherapy

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ABSTRACT: Adverse drug reactions (ADRs) remain a major global healthcare challenge, accounting for significant morbidity, mortality, treatment failure, and increased healthcare expenditure. Although clinical factors such as age, comorbidities, organ function, and polypharmacy contribute to ADR susceptibility, they inadequately explain the marked interindividual variability in drug response. Pharmacogenomics has emerged as a transformative approach to precision medicine by identifying inherited genetic variants that influence drug metabolism, transport, efficacy, and toxicity. This review critically examines the role of pharmacogenomic testing in predicting, preventing, and managing ADRs, with emphasis on clinically actionable pharmacogenes *including CYP2D6, CYP2C19, TPMT, NUDT15, HLA-B15:02, HLA-B57:01, and HLA-B 58:01.* Evidence from international pharmacogenomic guidelines demonstrates that genotype-guided prescribing significantly reduces severe hypersensitivity reactions, drug toxicity, and treatment failure while improving therapeutic efficacy and patient safety. The review further discusses current clinical applications, implementation challenges, ethical considerations, and emerging advances in genomic technologies, artificial intelligence, and clinical decision-support systems. The integration of pharmacogenomics into routine healthcare has the potential to optimize individualized drug therapy, minimize preventable ADRs, and accelerate the transition toward precision medicine, ultimately improving clinical outcomes and healthcare quality.

KEYWORDS: Pharmacogenomics; Adverse Drug Reactions; Precision Medicine; Pharmacogenetic Testing; Personalized Medicine.

INTRODUCTION

Global Epidemiology and Clinical Impact of Adverse Drug Reactions

Adverse drug reactions (ADRs) remain a major challenge to patient safety and are associated with considerable morbidity, mortality, prolonged hospitalization, and increasing healthcare expenditure worldwide. Earlier estimates suggested that ADRs contributed to more than 100,000 deaths annually in the United States; however, these findings were later questioned because the mortality estimates were derived from hospital admission data and ADR incidence reported over different study periods.[1,2] Despite these limitations, ADRs continue to represent a substantial burden on healthcare systems globally.

The rapid expansion of modern pharmacotherapy, including biologics, targeted therapies, immunotherapies, and combination treatment regimens, has further increased the complexity of drug safety assessment. Unlike conventional small-molecule drugs, the safety profiles of these therapies are often influenced by patient-specific factors and may not be completely characterized during pre-marketing clinical trials. Evidence from pharmacovigilance programs and post-marketing surveillance has demonstrated that several clinically significant toxicities become evident only after widespread clinical use, particularly following prolonged exposure or during combination therapy.[3] These observations indicate that drug safety should not be considered a fixed characteristic established at the time of regulatory approval but rather a dynamic outcome influenced by patient heterogeneity, treatment duration, comorbidities, and complex biological interactions.[4]

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Globally, ADRs account for a considerable proportion of hospital admissions and remain an important cause of preventable mortality in both developed and developing countries. Approximately 2.5–10.6% of hospital admissions in Europe and 3–6% in the United States are attributed to ADRs. In low- and middle-income countries, unsafe medical care is estimated to result in nearly 134 million adverse events annually, leading to approximately 2.6 million deaths.[5,6] Similarly, pharmacovigilance reports from the United Kingdom have shown a steady increase in reported ADRs over recent years, emphasizing the growing importance of continuous drug safety monitoring.[7]

Recent advances in pharmacogenomics have further expanded the understanding of ADR susceptibility by demonstrating that genetic variation significantly influences drug response. Conventional assessments of drug–drug interactions are therefore being extended to include drug–drug–gene interactions (DDGIs), particularly those involving clinically important pharmacogenes such as CYP2C9, CYP2C19, and CYP2D6, which substantially influence drug metabolism and toxicity.[8]

Limitations of "One-Size-Fits-All" Pharmacotherapy

Completion of the Human Genome Project marked a significant milestone in biomedical research and accelerated the development of precision medicine. Among its earliest clinical applications, pharmacogenomics emerged as a promising approach to replace the traditional "one-size-fits-all" model of drug therapy with individualized treatment strategies based on genetic variability.[9] The incorporation of pharmacogenomic information into drug prescribing has been increasingly supported by regulatory agencies, including the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA). The inclusion of pharmacogenomic information in the prescribing labels of drugs such as irinotecan and 6-mercaptopurine demonstrated the growing recognition of genotype-guided therapy, with similar recommendations subsequently expanding to additional medications, including warfarin.[10]

Considerable interindividual variability exists in both therapeutic efficacy and drug toxicity, resulting in substantial differences in treatment outcomes among patients receiving the same medication. While some individuals achieve optimal therapeutic benefit, others experience treatment failure or severe ADRs. Such variability arises from multiple interacting factors, including age, sex, disease characteristics, organ function, environmental exposures, concomitant medications, lifestyle factors such as smoking, and inherited genetic variants.[11] Although the precise contribution of each factor varies among individuals, genetic polymorphisms have emerged as one of the most important determinants of variability in drug metabolism, efficacy, and safety, providing the scientific foundation for personalized pharmacotherapy.[12]

Emergence of Pharmacogenomics in Precision Medicine

Pharmacogenomics has become a fundamental component of precision medicine by enabling individualized drug therapy based on a patient's genetic profile rather than relying on standardized treatment approaches. Variability in drug response has long been recognized in clinical practice, with marked differences in therapeutic efficacy, adverse drug reactions, and drug toxicity among patients receiving identical treatments. Advances in molecular genetics, completion of the Human Genome Project, high-throughput sequencing technologies, and genome-wide association studies (GWAS) have substantially improved the understanding of genetic factors influencing pharmacokinetics, pharmacodynamics, drug efficacy, and toxicity. Integration of genomic information into clinical decision-making allows optimization of drug selection and dosage while minimizing preventable ADRs and improving therapeutic outcomes.[13]

Despite considerable progress, several barriers continue to limit the routine clinical implementation of pharmacogenomics. These include inadequate clinician awareness, limited reimbursement policies, insufficient infrastructure for standardized genetic testing, underrepresentation of diverse populations in genomic databases, and challenges associated with integrating pharmacogenomic information into electronic health records and routine clinical workflows. Addressing these limitations through multidisciplinary collaboration, expanded genomic research, improved healthcare infrastructure, and evidence-based clinical guidelines will be essential for realizing the full potential of pharmacogenomics in precision medicine.[14]

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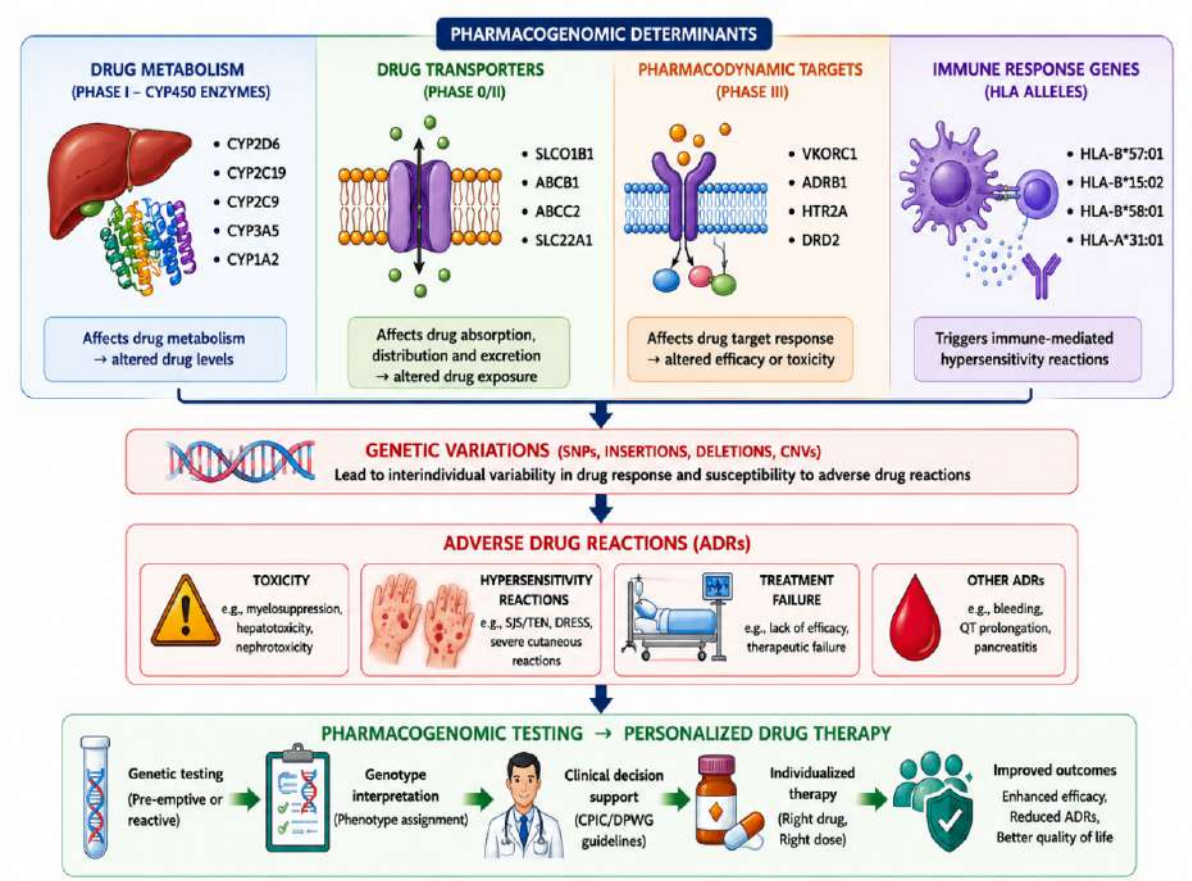

Fig No.1 : Pharmacogenomic determinants influencing adverse drug reactions and personalized drug therapy.

Classification of Adverse Drug Reactions and Genetic Influence

Type A and Type B Adverse Drug Reactions

Adverse drug reactions are broadly classified into Type A (Augmented) and Type B (Bizarre) reactions based on their underlying mechanisms and clinical characteristics. Type A reactions are dose-dependent, predictable, and result from an exaggerated pharmacological effect of a drug. They account for the majority of ADRs encountered in clinical practice and are generally associated with altered pharmacokinetic or pharmacodynamic responses. Since drug metabolism, transport, and receptor activity are influenced by genetic variation, pharmacogenomics plays an important role in identifying individuals at risk of these reactions. Consequently, pharmacogenetic testing has become increasingly valuable in optimizing drug selection and dosage, particularly in anticancer chemotherapy and other high-risk therapeutic areas.[15]

In contrast, Type B ADRs are uncommon, unpredictable, and usually unrelated to the normal pharmacological action or dose of the drug. These reactions frequently arise from genetic susceptibility or immune-mediated mechanisms and often present as severe hypersensitivity syndromes. Although some Type B reactions can now be predicted through pharmacogenomic screening, their biological mechanisms remain incompletely understood. Alterations in drug metabolism, drug targets, or immune recognition pathways may contribute to their development. In addition, inherited disorders such as glucose-6-phosphate dehydrogenase deficiency, porphyria, malignant hyperthermia, and drug-induced liver injury illustrate the significant contribution of genetic factors to idiosyncratic ADRs. Current evidence indicates that immune activation, particularly involving mast cells and T lymphocytes, plays a central role in many severe Type B reactions.[16,17]

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Table 1. Comparison of Type A and Type B Adverse Drug Reactions

Characteristic	Type A (Augmented) ADRs	Type B (Bizarre) ADRs
Definition	Exaggeration of the known pharmacological action of a drug	Unusual or idiosyncratic reactions not explained by the known pharmacological action
Frequency	Common	Relatively rare
Predictability	Generally predictable	Traditionally unpredictable
Dose relationship	Usually dose-dependent	Generally dose-independent
Underlying mechanism	Altered pharmacokinetic or pharmacodynamic response	Immune-mediated or genetically determined mechanisms
Major genetic influence	Variants affecting drug metabolism, transport, and drug targets	HLA alleles and immune-response genes
Important pharmacogenes	CYP2C9, CYP2C19, CYP2D6, TPMT, DPYD	HLA-B*15:02, HLA-B*57:01, HLA-B*58:01, HLA-A*31:01
Clinical consequence	Altered drug exposure, toxicity, or therapeutic failure	Hypersensitivity reactions including SJS, TEN, DRESS, and SCAR
Examples	Fluoropyrimidine toxicity associated with DPYD variants; thiopurine toxicity associated with TPMT variants	Abacavir hypersensitivity, carbamazepine-induced SJS/TEN, allopurinol-induced SCAR
Role of pharmacogenomics	Individualization of drug selection and dose optimization	Identification of genetically susceptible individuals and avoidance of high-risk drugs

Pharmacogenomics in Immune-Mediated and Idiosyncratic ADRs

Immune-mediated and idiosyncratic adverse drug reactions represent some of the most serious and clinically challenging forms of drug toxicity. Unlike Type A reactions, these events are generally unrelated to drug dose or pharmacological action and are predominantly influenced by host genetic factors, especially polymorphisms within the human leukocyte antigen (HLA) region. Advances in pharmacogenomics have significantly improved the understanding of these reactions by identifying genetic markers capable of predicting susceptibility before drug exposure. Consequently, genotype-guided prescribing has emerged as an effective strategy for preventing severe immune-mediated ADRs and improving patient safety.[18]

Immune-Mediated and Idiosyncratic ADRs

Immune-mediated ADRs occur when a drug or its reactive metabolite activates the adaptive immune system, resulting in either IgE-mediated immediate hypersensitivity or T-cell-mediated delayed hypersensitivity reactions. Most clinically significant pharmacogenomic associations involve delayed T-cell-mediated immune responses, in which HLA molecules present drug-derived antigens to T lymphocytes, triggering an exaggerated immune response and tissue injury.[19]

Drug Hypersensitivity Reactions

Drug hypersensitivity reactions comprise a broad spectrum of clinical manifestations ranging from mild cutaneous eruptions and fever to severe systemic syndromes involving multiple organs. Delayed hypersensitivity reactions are primarily mediated by drug-specific T cells, whereas certain reactions involve antibody-mediated or mast-cell-mediated immune mechanisms. Identification of strong associations between specific HLA alleles and severe hypersensitivity reactions has resulted in the development of international recommendations advocating pre-treatment HLA screening in genetically susceptible populations before initiating selected high-risk medications.[20,21]

Severe Cutaneous Adverse Reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) represent the most serious spectrum of immune-mediated adverse drug reactions and are associated with extensive skin and mucosal involvement, multisystem complications, and considerable mortality. The major clinical phenotypes include Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia

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and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP). Although these reactions occur infrequently, they are associated with significant clinical consequences, with mortality rates ranging from approximately 10% for SJS to 30–50% for TEN, emphasizing the importance of early diagnosis and preventive strategies.[22]

Genetic Basis of SCARs

Among all pharmacogenomic associations, human leukocyte antigen (HLA) polymorphisms provide the strongest evidence for the prevention of severe immune-mediated ADRs. Identification of susceptible individuals before initiating treatment has substantially reduced the incidence of life-threatening hypersensitivity reactions and represents one of the most successful clinical applications of precision medicine.[23]These pharmacogenomic associations clearly demonstrate the clinical value of genotype-guided prescribing in reducing severe immune-mediated ADRs and improving patient safety in routine clinical practice.[23]

Pharmacogenomic Determinants of Drug Safety

Pharmacogenomic determinants of drug safety comprise inherited genetic variations that modify an individual's susceptibility to adverse drug reactions by influencing drug pharmacokinetics, pharmacodynamics, and immune responses. These genetic determinants provide the biological basis for personalized medicine by enabling genotype-guided drug selection, dose optimization, and prediction of toxicity before treatment initiation. Mechanism-based classification into pharmacokinetic, pharmacodynamic**,** and **immunogenetic** variants provides a practical framework for understanding the role of pharmacogenomics in improving drug safety.[24]

Pharmacokinetic Genetic Variants

CYP450 Family of Drug-Metabolizing Enzymes

The cytochrome P450 (CYP450) enzyme family is responsible for the metabolism of a large proportion of clinically prescribed medications. Genetic polymorphisms within CYP2D6, CYP2C19, CYP2C9, and CYP3A5 produce metabolizer phenotypes that are classified as poor, intermediate, normal, or ultrarapid metabolizers, resulting in substantial interindividual variability in drug exposure and therapeutic response. These variations may increase the risk of drug toxicity or treatment failure depending on the medication involved. For example, reduced-function CYP2C9 alleles decrease warfarin metabolism and increase the risk of bleeding, whereas CYP2D6 ultrarapid metabolizers convert codeine more rapidly to morphine, thereby increasing susceptibility to opioid toxicity. Identification of these genetic variants enables individualized dose adjustment and improves treatment safety.[25,27]

Drug Transporter Genes: ABCB1 and SLCO1B1

In addition to drug-metabolizing enzymes, drug transporter proteins play a critical role in regulating drug absorption, tissue distribution, and elimination. Genetic polymorphisms in ABCB1 (P-glycoprotein) influence intestinal drug absorption, cellular efflux, and transport across the blood–brain barrier, thereby affecting drug disposition and clinical response. Similarly, the SLCO1B1 c.521T>C polymorphism reduces hepatic uptake of statins, resulting in increased plasma drug concentrations and a significantly higher risk of statin-associated myopathy. Current Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines recommend genotype-guided statin therapy for patients carrying high-risk SLCO1B1 variants to minimize adverse drug reactions while maintaining therapeutic efficacy.[28–30]

Pharmacodynamic Genetic Variants

Drug Receptors and Therapeutic Targets

Unlike pharmacokinetic variants, pharmacodynamic genetic variants alter the structure, function, or expression of drug targets without significantly affecting drug concentration. Consequently, these polymorphisms influence therapeutic efficacy and the risk of adverse drug reactions by modifying drug–target interactions. Variants in VKORC1 are well established as important determinants of warfarin sensitivity, whereas polymorphisms in OPRM1 and ADRB1 influence individual responses to opioid analgesics and β-blockers, respectively. Integration of pharmacodynamic markers with pharmacokinetic genotyping provides a more comprehensive strategy for optimizing drug therapy, improving treatment efficacy, and minimizing adverse drug reactions.[31]

Ion Channels and Intracellular Signaling Pathways

Genetic variants affecting ion channels and intracellular signaling pathways also contribute significantly to drug-induced toxicity. Polymorphisms in cardiac ion channel genes, including KCNH2, KCNE1, and SCN5A, increase susceptibility to drug-induced QT interval prolongation and torsades de pointes, thereby increasing the risk of potentially fatal cardiac arrhythmias. Similarly,

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pathogenic variants in RYR1 and CACNA1S predispose susceptible individuals to malignant hyperthermia following exposure to volatile anesthetics or succinylcholine. Identification of these variants before drug administration can substantially reduce the occurrence of severe drug-related complications and improve patient safety.[32,34]

Immunogenetic Variants

HLA Alleles and T-Cell-Mediated Adverse Drug Reactions

Among all pharmacogenomic biomarkers, human leukocyte antigen (HLA) polymorphisms represent the strongest predictors of severe immune-mediated adverse drug reactions. HLA molecules present drug-derived antigens to T lymphocytes, initiating immune activation that may result in delayed hypersensitivity reactions. Strong associations have been established between HLA-B*57:01 and abacavir hypersensitivity, HLA-B*15:02 and carbamazepine-induced Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and HLA-B*58:01 and allopurinol-induced severe cutaneous adverse reactions (SCARs). Implementation of pre-treatment HLA screening has significantly reduced the incidence of these potentially life-threatening reactions and is now considered a major success of precision medicine in routine clinical practice.[35,37]

High-Risk Drugs with Established Pharmacogenomic Evidence

Several medications have well-established pharmacogenomic evidence demonstrating that inherited genetic variation significantly influences both therapeutic efficacy and the risk of adverse drug reactions. Clinical guidelines developed by the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Dutch Pharmacogenetics Working Group (DPWG), and regulatory authorities such as the U.S. Food and Drug Administration (FDA) recommend genotype-guided prescribing for selected high-risk drugs. Implementation of these recommendations supports individualized drug selection, dose optimization, and prevention of severe ADRs, thereby improving overall patient safety.[38–40]

Cardiovascular Drugs

Warfarin

Warfarin remains one of the most extensively studied drugs in pharmacogenomics. Genetic polymorphisms in CYP2C9 and VKORC1 significantly influence warfarin metabolism and dose requirements. Reduced-function **CYP2C9 (*2 and 3)* alleles decrease metabolic clearance, increasing the risk of excessive anticoagulation and bleeding, whereas the VKORC1 −1639G>A polymorphism enhances warfarin sensitivity and lowers dose requirements. Genotype-guided dosing has been shown to improve anticoagulation control while reducing hemorrhagic complications.[41]

Clopidogrel

Clopidogrel is a prodrug that requires metabolic activation primarily by CYP2C19. Individuals carrying **loss-of-function CYP2C19 alleles (*2 and 3)* exhibit reduced formation of the active metabolite, resulting in diminished antiplatelet activity and an increased risk of recurrent cardiovascular events and stent thrombosis. Current CPIC guidelines recommend alternative P2Y12 inhibitors, including ticagrelor or prasugrel, for patients identified as poor metabolizers.[42]

Statins

Genetic variation in SLCO1B1, particularly the c.521T>C polymorphism, reduces hepatic uptake of simvastatin and increases systemic drug exposure, thereby predisposing patients to statin-associated myopathy. Genotype-guided statin selection and dose modification have been shown to reduce muscle toxicity while maintaining lipid-lowering efficacy.[43]

Neuropsychiatric and Antiepileptic Drugs

Carbamazepine

Carbamazepine-induced severe cutaneous adverse reactions have strong pharmacogenomic associations with HLA-B*15:02 and HLA-A*31:01. HLA-B*15:02 is closely associated with Stevens–Johnson syndrome and toxic epidermal necrolysis, particularly among Asian populations, whereas HLA-A*31:01 has been linked to DRESS syndrome, maculopapular eruptions, and other delayed hypersensitivity reactions. International guidelines recommend pre-treatment HLA screening before initiating carbamazepine therapy in genetically susceptible populations.[44–45]

Phenytoin

Phenytoin toxicity is influenced by both pharmacokinetic and immunogenetic factors. Reduced-function **CYP2C9** alleles decrease drug metabolism, whereas **HLA-B*15:02** markedly increases the risk of severe cutaneous adverse reactions, including Stevens–

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Johnson syndrome and toxic epidermal necrolysis. Current CPIC recommendations support genotype-guided dosing and HLA screening before initiating phenytoin therapy in high-risk individuals.[46]

Antidepressants

Genetic polymorphisms in CYP2D6 and CYP2C19 significantly influence the metabolism of tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs). Poor metabolizers are at increased risk of drug accumulation and adverse effects, whereas ultrarapid metabolizers may experience subtherapeutic drug concentrations and treatment failure. Pharmacogenomic-guided dose adjustment and individualized drug selection improve treatment response, reduce adverse drug reactions, and enhance the overall safety of antidepressant therapy.[47]

Clinical Implementation of Pharmacogenomic Testing

Pharmacogenomic (PGx) testing is increasingly being integrated into routine clinical practice to improve medication safety, reduce adverse drug reactions (ADRs), and support precision medicine. Effective implementation requires appropriate testing strategies, accurate interpretation of genetic variants, and integration of pharmacogenomic information into electronic health records (EHRs) supported by clinical decision support (CDS) systems. International organizations such as the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG) have developed evidence-based guidelines to facilitate genotype-guided prescribing and standardize the clinical implementation of pharmacogenomics.[48]

METHODS OF TESTING

Reactive vs. Pre-emptive Pharmacogenomic Testing

Reactive pharmacogenomic testing is performed after drug initiation, usually following an adverse drug reaction or an unexpected therapeutic response.In contrast, pre-emptive pharmacogenomic testing involves genotyping multiple clinically relevant pharmacogenes before drug therapy is required. The patient's genetic information is stored in the electronic health record (EHR) and remains available throughout life to guide future prescribing decisions. The multicentre PREPARE study demonstrated that pre-emptive panel-based pharmacogenomic testing significantly reduced clinically relevant adverse drug reactions compared with standard care, supporting its clinical value in routine practice.[49]

Single-Gene vs. Panel-Based Testing

Single-gene testing is appropriate when a specific drug–gene interaction is anticipated, such as HLA-B*57:01 screening before initiating abacavir therapy.In contrast, panel-based testing simultaneously evaluates multiple clinically actionable pharmacogenes, including CYP2D6, CYP2C19, CYP2C9, SLCO1B1, TPMT, NUDT15, DPYD, and selected HLA alleles. This approach offers greater clinical utility for patients likely to receive multiple medications by eliminating repeated genetic testing and has become increasingly incorporated into precision medicine programs.[50]

Interpretation and Clinical Decision Support

Assigning Phenotypes

Following genotyping, identified genetic variants are translated into clinically relevant metabolizer phenotypes, including poor, intermediate, normal, rapid, and ultrarapid metabolizers. These standardized phenotype classifications are used by CPIC and DPWG to guide individualized drug selection and dose adjustment, ensuring consistent interpretation across clinical laboratories and healthcare settings.[51]

Integration with Electronic Health Records

Integration of pharmacogenomic information into electronic health records (EHRs) together with clinical decision support (CDS) systems enables automated prescribing alerts and genotype-guided therapeutic recommendations at the point of care. CDS systems assist clinicians by identifying gene–drug interactions, recommending dose modifications, suggesting alternative medications when appropriate, and reducing medication-related harm. This integration improves adherence to pharmacogenomic recommendations and supports safer prescribing practices.[52]

Evidence-Based Guidelines and Regulatory Landscape

CPIC and DPWG Recommendations

The Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG) have developed evidence-based guidelines that translate pharmacogenomic test results into practical prescribing recommendations. These guidelines currently include more than 90 clinically actionable gene–drug pairs and provide recommendations regarding drug

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selection, dose adjustment, or alternative therapy according to an individual's genotype. They form the foundation for the global clinical implementation of pharmacogenomics.[53]

Pharmacogenomic Labeling by the FDA and EMA

The U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) incorporate pharmacogenomic information into drug labeling for medications with established gene–drug associations. Depending on available evidence, regulatory labeling may recommend or require genetic testing before therapy, including HLA-B*57:01 for abacavir, DPYD for fluoropyrimidines, and TPMT/NUDT15 for thiopurines. However, differences remain among the FDA, EMA, CPIC, and DPWG recommendations, emphasizing the need for greater international harmonization of pharmacogenomic guidelines.[54]

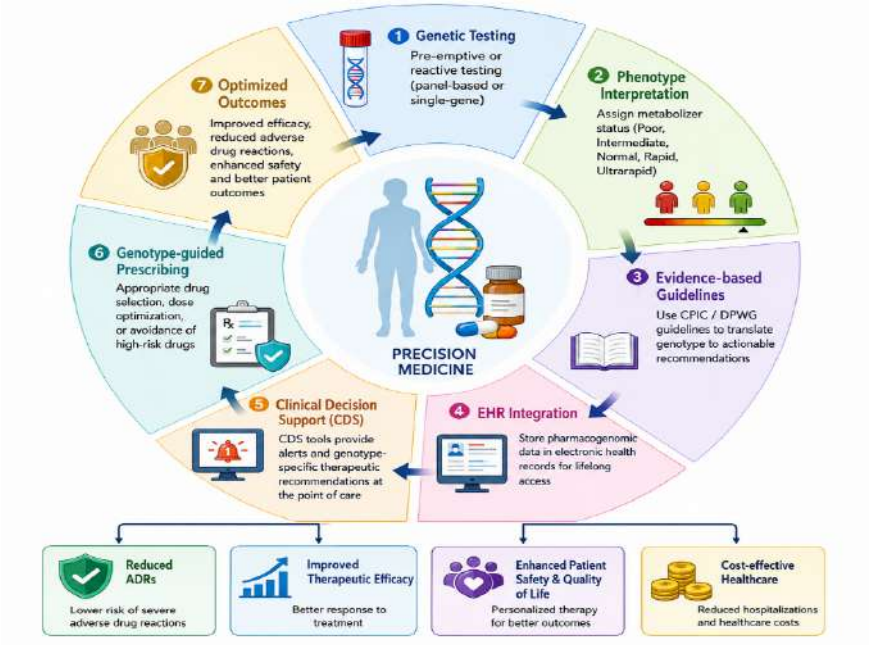

Fig No. 2: Integration of pharmacogenomics into clinical practice through genetic testing, phenotype interpretation, evidence-based guidelines, electronic health records, clinical decision support, and genotype-guided prescribing to improve medication safety and therapeutic outcomes.

Economic and Public Health Impact of Pharmacogenomics

Cost-Effectiveness of Pharmacogenomic Testing

Pharmacogenomic (PGx) testing has been shown to be cost-effective, particularly for medications with established gene–drug interactions. Pre-emptive panel-based testing can prevent severe adverse drug reactions (ADRs), reduce unnecessary medication changes, and lower long-term healthcare costs. Economic studies have demonstrated that although the initial cost of testing may be considerable, its long-term clinical and economic benefits frequently outweigh these expenses, especially among patients receiving multiple medications.[55]

Reduction in Hospitalization and Healthcare Costs

Genotype-guided prescribing significantly reduces preventable adverse drug reactions, thereby decreasing hospital admissions, emergency department visits, treatment discontinuation, and overall healthcare expenditure. Evidence from the multicentre PREPARE study demonstrated that pre-emptive pharmacogenomic testing significantly reduced clinically relevant ADRs compared with standard care, highlighting its role in improving patient safety and optimizing healthcare resource utilization.[56]

Ethical, Legal, and Social Implications (ELSI)

Genetic Privacy and Data Security

Pharmacogenomic testing generates sensitive genetic information that requires protection against unauthorized access, misuse, and genetic discrimination. Secure storage of genomic data, restricted access, and compliance with data protection regulations are

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essential to maintain patient confidentiality and public trust. As pharmacogenomic information becomes increasingly integrated into electronic health records, ensuring data security and responsible data sharing remains a major ethical priority.[57,58]

Informed Consent

Obtaining informed consent before pharmacogenomic testing is essential. Patients should receive adequate information regarding the purpose of testing, expected clinical benefits, potential limitations, incidental findings, and the future storage and use of their genetic information. Appropriate pre-test counselling promotes informed decision-making and supports the responsible implementation of pharmacogenomics in precision medicine.[59]

CONCLUSION

Pharmacogenomics has emerged as a cornerstone of precision medicine by identifying genetic variants associated with adverse drug reactions and interindividual variability in drug response. Strong evidence linking polymorphisms in CYP450 enzymes, drug transporters, pharmacodynamic targets, and HLA alleles with drug toxicity has enabled genotype-guided prescribing for several high-risk medications, including warfarin, clopidogrel, carbamazepine, abacavir, thiopurines, and fluoropyrimidines. Consequently, pharmacogenomic testing has significantly improved medication safety by optimizing drug selection, individualizing dosage, and reducing preventable adverse drug reactions.Future integration of pre-emptive panel-based pharmacogenomic testing, clinical decision support systems, and national precision medicine initiatives is expected to accelerate the routine application of pharmacogenomics in clinical practice. Continued research, international harmonization of pharmacogenomic guidelines, and supportive healthcare policies will be essential to establish pharmacogenomics as a standard component of safe and effective drug therapy, ultimately reducing the global burden of adverse drug reactions and improving patient outcomes.

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