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Pharmacogenomics In Neonatal Care: Tailoring Drug Therapy Based on Genetic Profiles in Infants

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ABSTRACT

Neonatal pharmacotherapy remains a clinical challenge due to the immaturity of organ systems and the absence of robust age-specific pharmacokinetic and pharmacodynamic data. As most drugs used in Neonatal Intensive Care Units(NICUs) are prescribed off-label, there is a heightened risk of adverse drug reactions, therapeutic inefficacy, and unpredictable dosing. Pharmacogenomics, the study of how genetic variation influences drug response, offers a promising strategy to individualize therapy in neonates. However, its application in this vulnerable population is complicated by ontogeny, the dynamic kinetics of metabolic enzymes and transport systems. This review explores the fundamental principles of pharmacogenomics in the neonatal context, detailing gene-drug interactions of clinical significance involving CYP450 enzymes, uridine diphosphate glucuronosyltransferases (UGTs), thiopurine methyltransferase (TPMT), Dihydropyrimidine dehydrogenase (DPYD) and transporters. The current genomic tools, such as next-generation sequencing and point-of-care genotyping, address implementation barriers, including ethical considerations, data interpretation challenges, and provider preparedness are evaluated in this review. Real-world applications, such as the prevention of aminoglycoside-induced cytotoxicity and optimization of sedative dosing, highlight the clinical value of early genotyping. Looking forward, the integration of electronic health records, AI-driven decision support, and neonatal-specific pharmacogenomic databases will be pivotal in mainstreaming personalized medicine in NICUs. Pharmacogenomics thus holds the potential to reshape neonatal care by improving drug safety, efficacy, and health outcomes since the earliest stages of life.

Keywords: *Pharmacogenomics, Neonates, Precision medicine, CYP450, Personalized therapy, Neonatal drug metabolism*

1. INTRODUCTION

Among all clinical pharmacotherapies, neonatal pharmacotherapy is considered to be one of the most sensitive and tough due to the immaturity of vital organ systems, as well as to the relatively inadequate amount of age-specific pharmacokinetic and pharmacodynamic data. Most prescribed medications in neonatal intensive care units (NICUs) are indeed prescribed off-label, more often with dosages extrapolated from adult or pediatric populations and leading to increased risk for adverse drug reactions, therapeutic failures, and dosing.[1]Highly variable and evolving metabolic capabilities cause this population to react to commonly used medications in a wide range of ways. Neonates possess immature liver and kidney function as well as underdeveloped drug transport mechanisms and dynamic changes in body composition, which make them susceptible to either inadequate exposure to a drug or the toxic accumulation of a drug.[2] In most cases, well-designed and conducted clinical trial data specific to the neonate are lacking due to ethical concerns and logistical problems, making strong evidence-based dosing recommendations difficult and frequent reliance on empirical treatment strategies that might not be reflective of the unique needs and biological differences of the neonate.[3]

Pharmacogenomics is one of the most important tools of the precision medicine era. The term is used as a tool for individualized drug therapy based on some genetic variations that alter the absorption, distribution, metabolism, and excretion of a drug.[4] These genetic variants may influence cytochrome P450 enzymes activity, drug transporters, receptors, and conjugating enzymes, and determine the pharmacological efficacy and toxicity of drugs. Based on this knowledge, personalized drug regimens have emerged in diverse fields ranging from oncology and psychiatry to cardiology for the benefit of pharmacogenomic-guided therapies.[5] The genes CYP2C19, CYP2D6, and VKORC1 have been well characterized for their contribution to drug metabolism and are already known to influence clinical practice in both adults and children.[6] Applying pharmacogenomic data at the neonatal age is not straightforward because the developmental trajectory of gene expression modifies the phenotypic effect of genetic polymorphisms.

Metabolic enzymes and transport systems have a rapid and non-linear ontogeny, and neonates represent a distinct pharmacogenomic population.[7] For example, the key drug metabolism enzyme CYP3A4 is virtually inactive at birth and increases slowly through the first year of life, whereas CYP3A7 is highly expressed during fetal life and decreases postnatally. Likewise, mechanisms of renal drug clearance mature over weeks to months, affecting drugs cleared by glomerular filtration and tubular secretion.[8]A pharmacogenomic variant for a gene in a neonate can have a radically different effect from older individuals since that gene is unlikely to be fully expressed yet. Hence, it is important to combine genetic data with developmental biology to interpret pharmacogenomic test results in neonatal care.[9]

Neonates have altered immune responses, reduced plasma protein binding, immature blood-brain barriers, and unique disease profiles, further uniquely defining their pharmacologic response to drugs. Due to the possibility of gene-environment and gene-age interactions, the conventional pharmacogenomic algorithm should be reevaluated, in application to this population.[10] Medications such as phenobarbital, caffeine, and morphine for conditions such as neonatal seizures, apnea of prematurity, and respiratory distress syndrome are affected by genetic polymorphisms in genes such as CYP2C9, ADORA2A, and UGT2B7, respectively.[11] Additionally, neonates have presented with adverse reactions such as aminoglycoside-induced cytotoxicity, and mitochondrial DNA mutations have been identified to be causative.

These associations are known, but pharmacogenomics has been minimally incorporated into neonatal clinical care.[12] Few barriers include a lack of neonatal-specific genotype-phenotype databases, limited awareness among healthcare professionals, cost and accessibility to genetic testing, and ethical concerns regarding collecting genetic data in this group.[13] Despite this, pilot studies and case reports conducted recently indicate that pharmacogenomic-guided dosing can improve therapeutic outcomes, decrease hospital stays, and decrease medication-related adverse events in the neonate.[14]. A case reported in neonatal with ocular and neurological abnormalities confirmed DPD enzyme lacking corroborated with point mutation (DPYD*2A). Next-generation sequencing, point-of-care genotyping, and integrative bioinformatics tools, which are all emerging technologies, are making genetic profiling quicker and more affordable, enabling it to be used in NICUs across the world.[15]

The goal of this review is to determine how genetic profiling can be used to individualize drug therapy and improve therapeutic efficacy, as well as reduce adverse outcomes in neonates. This study is based on a critical review of the current literature and clinical practices and aims to bring a foundation for incorporating pharmacogenomic approaches in neonatal intensive care, ultimately improving precision medicine in this highly vulnerable population.

2. FUNDAMENTALS OF PHARMACOGENOMICS

Pharmacogenetics and pharmacogenomics are related concepts, but define two different aspects of genetics, i.e. drug response relationship. Traditionally, pharmacogenetics has addressed the effect of a single gene variant on drug metabolism and response, but in the context of inherited disorders. Unlike pharmacogenomics, pharmacogenetics is geared to focus on an individual variant that is presumed to affect drug efficacy, safety, or dosing.[16] As developmental biology and genetic variation have big impacts on pharmacologic outcomes in this setting, this holistic perspective is becoming increasingly important in the care of neonates.

All aspects of drug disposition or ADME (absorption, distribution, metabolism, and excretion) can be modulated genetically. Medication processing is influenced by variants in genes encoding drug-metabolizing enzymes (e.g., genes of the CYP450 family), transporters (e.g., ABCB1, SLCO1B1), and drug targets (e.g., receptors, ion channels) in neonates.[17] Taking a classic example, such polymorphisms can decrease the enzyme activity and have prolonged drug half-life and increased toxicity, or increase metabolism and reduce sub therapeutic drug exposure. The effects of these are especially significant in neonates whose enzymatic systems are not mature and often do not function likethose of older children and adults.[18]

The cytochrome P450 (CYP) enzymes, which constitute a key family of genes involved in neonatal pharmacogenomics, are responsible for the oxidative metabolism of a large number of drugs.[19] Uridine diphosphate glucuronosyltransferases (UGTs) contribute to the phase II reactions of glucuronidation as detoxifying enzymes, and thiopurine methyltransferase (TPMT) is needed for the metabolization of labelled thiopurine drugs.[20] These enzymes are ontogenically changing, which means that their expression levels change over time, and therefore, the clinical relevance of variants in these genes in terms of neonatal development is not well understood.

There are several polymorphisms that are important in the neonate. Table 1 presents the summary of genetic polymorphisms influencing drug metabolism in neonates.

Table 1: Clinically Relevant Genetic Polymorphisms Influencing Drug Metabolism in Neonates

Gene	Polymorphism (Allele Variant)	Associated Drug(s)	Effect on Drug Metabolism	Clinical Implications in Neonates	Population Frequency / Notes
CYP2D6	CYP2D6 *3, *4, *10, *41	Codeine, Tramadol	Decreased or absent enzyme activity	Risk of respiratory depression due to morphine buildup	CYP2D6 10 common in Asians[21]
CYP2C9	CYP2C9 *2, *3	Phenytoin	Reduced metabolic clearance	Increased neurotoxicity at standard doses	CYP2C9 3 seen in Caucasians[22]
CYP3A5	CYP3A5 *3, *6, *7	Midazolam, Tacrolimus	Decreased enzymatic expression	Altered sedation and immunosuppressive levels	High in African populations[23]
UGT1A1	UGT1A1 *28	Morphine, Irinotecan	Impaired glucuronidation	Hyperbilirubinemia and morphine toxicity	Linked to neonatal jaundice[24]
TPMT	TPMT *2, *3A, *3C	Mercaptopurine, Azathioprine	Low enzyme activity	Myelosuppression, increased toxicity	Genetic screening before therapy is recommended[25]
SLCO1B1	SLCO1B1 *5, *15	Statins, Ceftriaxone	Reduced hepatic uptake	Elevated plasma drug levels, bilirubin competition	Rare in neonates but clinically relevant[26]
ABCB1	3435C>T	Digoxin, Morphine	Altered efflux transport	CNS drug accumulation, variable sedation	Affects blood-brain barrier penetration[27]

NAT2	Slow acetylator alleles	Isoniazid, Hydralazine	Slower metabolism	Higher risk of toxicity	Relevance for congenital TB cases[28]
CYP1A2	CYP1A2 *1F, *1C	Caffeine	Reduced enzyme activity in neonates	Prolonged half-life, apnea treatment modulation	Activity low at birth regardless of genotype[7]
DPYD	DPYD*2A	Anti-neoplastic drugs, 5FU	Lower DPD enzyme activity in neonates	Ocular abnormalities, high grade of toxicity	DPYD*2A 3% (heterozygous) in Caucasians, 4 % in Finnish[66]

3. UNIQUE PHARMACOKINETICS AND PHARMACODYNAMICS IN NEONATES

Pharmacokinetic and pharmacodynamic differences between older children and adults are profound,as key physiological systems are immature in neonates. At birth, hepatic and renal functions are underdeveloped and are the primary pathways for drug metabolism and elimination. Unlike the cytochrome P450 (CYP) family and conjugation systems such as UGT and SULT, the activity of key metabolic enzymes is minimal in the neonatal liver, which slows drug biotransformation.[8] For example, the expression of CYP3A4 and UGT1A1, important in metabolizing midazolam and bilirubin, respectively, is low in the neonate, leading to drug accumulation and toxicity.[29]

Renal function during the newborn period is also markedly immature, having progressive development of glomerular filtration rate (GFR), tubular secretion, and reabsorption along the first year of life. Drugs that are cleared renally (e.g., aminoglycosides and beta-lactams) can have prolonged half-lives, and dosing adjustments must be made to avoid toxicity.[30] Drug distribution volumes and plasma concentrations are thus greatly influenced by these immature excretory mechanisms, altered body water content, and reduced protein binding.

Developmental changes in gene expression over time are important in neonatal pharmacogenomics due to its concept of ontogeny. The enzyme activity is not constant during the neonatal period. CYP1A2 is hardly detectable at birth and is detectable by 1–3 months of age, and affects the metabolism of caffeine and related drugs.[7] Drug absorption and tissue penetration are altered by the dynamic expression of transporters and receptors, in particular, the very permeable blood-brain barrier of neonates.

These age-related variations affect all parts of ADME. Higher gastric pH can, additionally, slow drug absorption by delaying the emptying of the drug from the stomach. A greater degree of total body water and lower fat affect distribution. Enzyme limitation controls metabolism, and renal function is insufficiently developed for excretion.[31]It is important to know both the genetic and developmental factors that determine drug handling for proper pharmacotherapy in this vulnerable population.Immature liver and kidney functions, age-dependent enzyme expression, and ontogeny-influenced gene activity, which affect drug absorption, distribution, metabolism, and excretion, are the causes of variability in neonatal pharmacokinetics and pharmacodynamics, and these are illustrated in Figure 1.

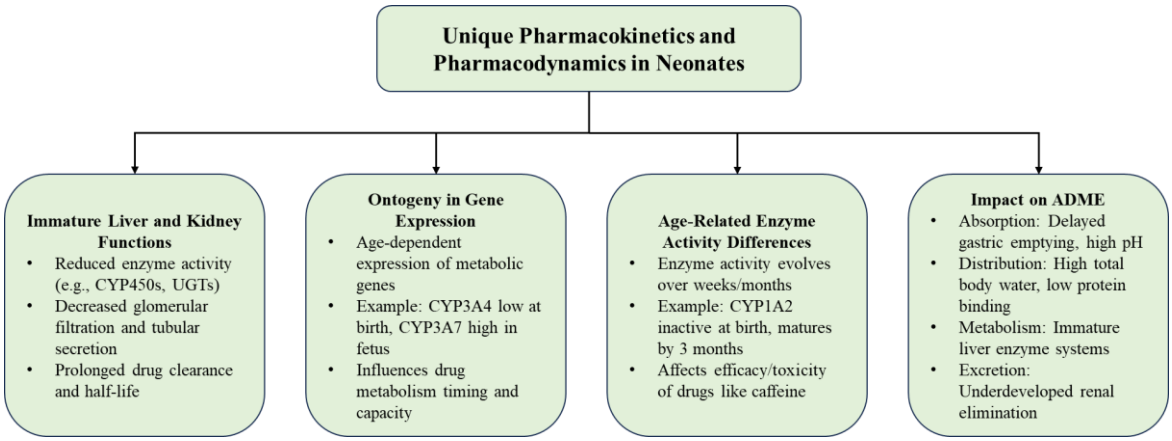

Figure 1: Determinants of Pharmacokinetic and Pharmacodynamic Variability in Neonates: Implications for Drug Therapy

4. PHARMACOGENOMIC VARIANTS AND COMMON NEONATAL DRUGS

There has been significant advancement of pharmacogenomic insight to personalized adult drug therapy, whereas its application in neonatal care settings remains emerging. Increasing evidence indicates that genetic polymorphisms in neonates can impact response to drugs, drug metabolism, and toxicity.[32] More and more key gene drug associations in commonly used neonatal medications are being recognized.

Morphine and other analgesics and sedatives are metabolized via uridine 5′-diphospho-glucuronosyltransferase 2B7 (UGT2B7) and work through the μ-opioid receptor encoded by OPRM1. OPRM1 A118G polymorphism can alter receptor affinity and thus affect analgesic responses, and UGT2B7 polymorphisms impair morphine clearance, making the patient more prone to respiratory depression when given morphine.[14] The sedative midazolam is metabolized by CYP3A5, and this enzyme has decreased clearance in neonates with the CYP3A5 *3/*3 genotype, leading to drug accumulation and prolonged sedation.[33]

One of the antibiotics, aminoglycosides such as gentamicin, has a risk of irreversible ototoxicity in neonates who carry the m.1555A>G mitochondrial mutation.[34] Such adverse outcomes can be prevented by preemptive genetic testing. β-lactam pharmacokinetics may be affected by polymorphisms in renal transporter genes SLC22A6/8.

Polymorphisms of CYP2C9 and CYP2C19 for anticonvulsants (phenytoin) affect metabolism, and reduced function alleles may cause toxicity. There is also emerging data that genetic variability may affect levetiracetam response.[35]In cardiovascular therapy, variants of CYP2C8/2C9 change prostaglandin E1 metabolism, and polymorphisms of ADRB1/ADRB2 alter beta-blocker effect. Caffeine metabolism is required for respiratory support, but due to low neonatal CYP1A2 expression, its impact on treatment is limited; ADORA2A variants may affect treatment sensitivity.[36] The pharmacogenomic screening of these gene-drug relationships to optimize neonatal therapeutics and reduce risk. The pharmacogenomic variants and common neonatal drugs are mentioned in Table 2.

Table 2: Pharmacogenomic Variants and Common Neonatal Drugs

Drug Class	Drug	Relevant Gene(s)	Polymorphism	Effect on Drug Response	Clinical Relevance in Neonates
Analgesics & Sedatives	Morphine	OPRM1, UGT2B7	A118G, UGT2B7 variants	Altered receptor binding and metabolism	Risk of sedation or respiratory depression[37]
	Midazolam	CYP3A5	*3/*3 (non-expresser)	Reduced metabolism, drug accumulation	Prolonged sedation[38]
Antibiotics	Gentamicin	MT-RNR1 (mitochondrial gene)	m.1555A>G	Enhanced cochlear toxicity	Increased risk of ototoxicity[39]
	Cefotaxime	SLC22A6/8	Transporter variants	Modified renal clearance	Altered half-life[40]
Anticonvulsants	Phenytoin	CYP2C9, CYP2C19	*2/*3 (loss-of-function)	Reduced clearance, toxicity risk	CNS side effects, dose adjustment required[41]
	Levetiracetam	SV2A, SLC transporters	Emerging variants	Under investigation	Interindividual variability[35]
Cardiovascular Agents	Prostaglandin E1	CYP2C8, CYP2C9	Reduced-function alleles	Altered metabolism	Efficacy modulation[42]

	Propranolol	ADRB1, ADRB2	Arg389Gly, Gly16Arg	Variability in receptor sensitivity	Differences in HR response and BP control[43]
Respiratory Support	Caffeine	CYP1A2, ADORA2A	*1F, 1976C>T	Delayed metabolism, altered receptor binding	Dosing variability, apnea control[44]

5. TECHNOLOGIES AND TOOLS IN NEONATAL PHARMACOGENOMICS

Genomic technologies have greatly advanced the feasibility of integrating pharmacogenomics into neonatal clinical care. Importantly, Next Generation Sequencing (NGS) technology in particular demonstrates a high throughput and provides wide coverage of the sequencing region. The simultaneous analysis of multiple genes involved in drug metabolism, transport, and response can be performed by NGS, and the method is capable of revealing rare or novel variants that are relevant to neonatal pharmacotherapy.[45] Whereas traditional single-gene assays determine only one gene at a time, whole-exome and targeted gene panel sequencing reveal actionable variants in CYP450 enzymes and UGTs and mitochondrial genes in a clinically relevant timeframe.

There is, however, a rapid and focused alternative, targeted point-of-care genotyping platforms. Typically, these are systems based on PCR or microarray technologies that have been designed for detecting known single-nucleotide polymorphisms (SNPs) with established clinical significance. The platforms, IDgenetix® and GeneSight®, can give neonatal intensive care units such as the NIFTY study, can give newborns results within a few hours, which can help with the personalization of medications like phenytoin, morphine, and caffeine. Their utility is limited by fixed variant panels and they can potentially miss rare or population-specific variants that impact drug response.[46]

The reading and understanding of pharmacogenomic data require sophisticated bioinformatics tools for combining the variant data with clinical decision-support systems. Primarily based on genotypic data, genotype-driven algorithms enable the translation into phenotype predictions and therapeutic recommendations.[47] This can be attained with the aid of platforms such as PharmGKB, CPIC guidelines, and ClinVar. In neonates, the algorithms need to take into account gene expression in development and use age-appropriate pharmacokinetic models. Such tools are becoming increasingly relevant in context through recent efforts to create pediatric pharmacogenomic ontologies.[48]

Cost, turnaround time, and accuracy are still considered to be the key factors in clinical adoption. Although NGS and array-based genotyping have become less expensive, cost and limited insurance coverage act as barriers in many healthcare settings.[49] The turnaround times have been improved so that some laboratories can deliver the comprehensive panel within 48-72 hours.

6. CLINICAL IMPLEMENTATION CHALLENGES

Despite the challenges of ethical, infrastructural, and educational hurdles, pharmacogenomics has a successful opportunity to be implemented in neonatal care provided that safe and effective clinical application is guaranteed.[18] The central ethical issue is that of informed consent for genetic testing in neonates. Given that neonates cannot provide assent, the responsibility of assenting to research lies with the parents or guardians, who must decide on complex and often unfamiliar genomic concepts.[50] The concerns are concerning the scope of consent, particularly concerning incidental findings that may be found. Besides, long-term storage and secondary use of genetic data also pose questions about whether the child would be the owner of the data in his/her adulthood or would have to seek consent again, and the child's right to privacy.

There are currently limited pharmacogenomic reference data and genotype–phenotype correlation data available for other neonatal diseases for which a targeted treatment approach may be warranted.[51] For most established pharmacogenomic associations, studies in adults or older children were used, whose drug metabolism profiles differ greatly from neonates because of developmental immaturity. The lack of age-appropriate data for pharmacogenomic tests makes its clinical applicability in neonates uncertain, as dosage adjustments or therapeutic predictions cannot be made.[52] Additional confounding variables that influenceare prematurity, other concurrent illnesses, environmental exposures, or epigenetic regulation. These factors reinforce the need for the use of multifactorial (developmental biology + pharmacogenomic) approaches for better prediction accuracy and minimizing the adverse drug reactions [53]

NICUs in clinical practice often have operational limitations that make seamless adoption of pharmacogenomic testing impossible.[46] Delayed test results and a lack of integrated clinical decision-support systems are the factors that limit time-sensitive decision-making. In high-pressure environments, genotype-guided prescribing is impractical in the absence of EHR compatibility and real-timealerts [53]

Finally, there is a bottleneck in the limited pharmacogenomic literacy among healthcare providers. Multidisciplinary, structured education is necessary for clinicians to provide the requisite knowledge and confidence to interpret and responsibly apply genetic data in the context of neonatal care. The clinical implementation challenges of pharmacogenomics in neonatal care are illustrated in Figure 2.

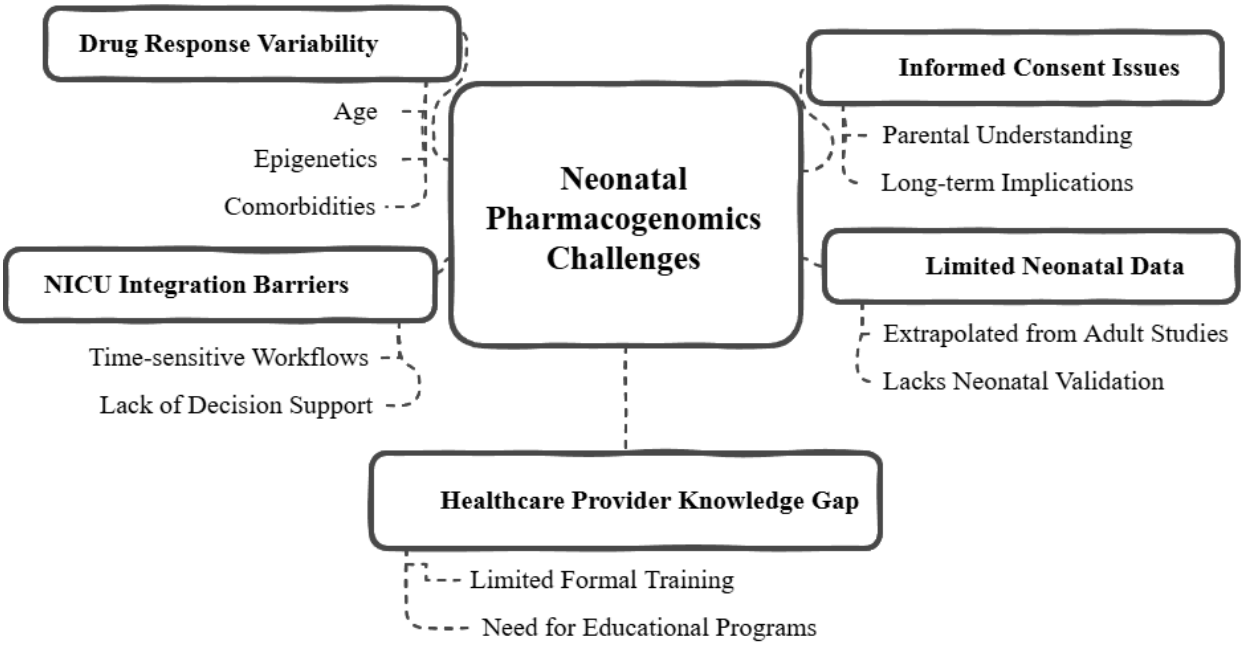

Figure 2: Barriers to Clinical Implementation of Pharmacogenomics in Neonatal Care

7. CASE STUDIES AND REAL-WORLD APPLICATIONS

A growing number of real-world case series and pilot studies have progressed the integration of pharmacogenomics as a practical feature in neonatal intensive care units (NICUs) from theoretical promise. Early implementations of these technologies provide important evidence for how genetic information can inform therapy and enhance outcomes in the neonate under a variety of clinical scenarios.

One of the most well-documented applications is mitochondrial DNA screening to prevent aminoglycoside-induced ototoxicity in neonates. Point-of-care genetic testing for the m.1555A>G mutation was employed in a landmark study at Manchester University NHS Foundation Trust for acutely ill neonates requiring aminoglycoside antibiotics in the UK. The test produced results within 30 minutes using a loop-mediated isothermal amplification (LAMP) assay. The test was applied to over 750 neonates and identified three carriers, enabling immediate substitution of antibiotics and thus avoiding irreparable hearing loss. The study found that rapid genotyping is possible, safe, and can be cost-effective by preventing lifelong disability and its associated healthcare costs.[54]

Later in the US, the IGNITE PGx (Implementing Genomics in Practice) project evaluated the integration of pharmacogenetic testing into different clinical settings, including NICUs.[55] While most data came from adult populations, TPMT and NUDT15 genotyping were shown to be feasible on a routine basis in children, including neonates treated with thiopurines for early life leukemia or immune conditions, at pediatric arms such as St. Jude Children's Research Hospital. Modification of dosing and reduced myelotoxicity were achieved without sacrificing therapeutic efficacy (implementation). .[56]

A study was performed in the Netherlands about sedative use and CYP3A5 genotyping for midazolam metabolism in neonates requiring mechanical ventilation.[38] The findings of the study showed that neonates with non-functional CYP3A5 genotypes (*3/*3) had significantly higher midazolam plasma concentrations and longer sedation duration and increased need for respiratory support than expressers. This resulted in recommendations for dose adjustment by genotype that might reduce the risk of sedation and NICU resource utilization [57]

Additional evidence from the Mayo Clinic's RIGHT 10K pharmacogenomics implementation program confirms the value of embedding pharmacogenetic data into the electronic health record (EHR) with an automated clinical decision support for improving drug selection, even for emergency and neonatal cases.[58]Even though the program covered all age groups, the availability of genotype information early in the transfer of neonates from maternity wards to NICUs was particularly beneficial in the use of opioids or anticonvulsants.[59]

In addition to efficacy and safety, neonatal pharmacogenomic interventions are cost-effective. Pre-emptive TPMT testing in neonates on thiopurine therapy was estimated to save $3,000 per patient from the U.S. perspective through avoiding hospitalization and treatment of severe adverse events. Consequently, m.1555A>G testing at birth was found to be cost-saving when compared with the lifetime cost of caring for hearing loss versus the relatively inexpensive upfront cost of genetic testing.[60]

Collectively, these examples underscore that, technically, pharmacogenomic testing in a neonate is possible and that the testing may also be clinically meaningful. Integrating the use of genotype into prescribing, especially in high-risk drug classes including aminoglycosides, sedatives, and immunosuppressants, promotes patient safety, enhances therapeutic outcomes, and provides a strong return on investment.

8. FUTURE PERSPECTIVES

The future for pharmacogenomics in neonatal care will depend on its integration into clinical workflows without requiring any additional effort, leveraging advanced informatics and a robust regulatory framework. The incorporation of pharmacogenomic data into EHRs that have real-time clinical decision support systems is one of the most promising developments. It makes it possible to send automated alerts and drug recommendations based on a neonate's genetic profile to clinicians at the point of care. According to a case series with early adopters of EHR-integrated pharmacogenomics, such as the Mayo Clinic and St. Jude Children's Research Hospital, this model is feasible as well as impactful on both medication safety and individualized dosing paradigms for all ages, even neonates.[61]

Artificial intelligence (AI) and machine learning are also on the brink of changing the neonatal pharmacogenomics landscape. Analysis of large-scale multi-omic data along with clinical variables using AI algorithms can accurately predict drug responses, drug adverse effects, and optimal dosing regimens compared to traditional models. In particular, in neonates, developmental physiology makes the prediction of complex physiology especially difficult, but well suited to AI (Topol, 2019).[62,63]

There is an increasing demand for neonatal-specific pharmacogenomic databases. While PharmGKB and CPIC are based on adult or pediatric populations, they lack the needed granularity for neonatal interpretation of variability. The development of age-stratified databases would help in improving genotype–phenotype correlations and aiding the refinement of neonatal dosing guidelines.[64]

Standardised implementation protocols and policy frameworks for such global initiatives are being developed by CPIC as well as the U-PGx (European Ubiquitous Pharmacogenomics) consortium. The efforts seek to ensure equitable access to pharmacogenomic-guided therapy across healthcare systems and to prevent the ethical use of genetic data.[65]

9. CONCLUSION

This review describes how the integration of pharmacogenomics into neonatal practice is a transformative opportunity to implement pharmacogenetics. Unlike older populations, neonates have great interindividual variability in drug response that can result from immature organ systems and also developmental changes in gene expression, as well as a lack of age-specific pharmacokinetic data. Pharmacogenomics, by unearthing the effects of particular genetic polymorphisms (e.g., CYP450 enzymes, UGTs, TPMT, and mitochondrial genes), allows for more accurate predictions of neonates in terms of drug metabolism, efficacy, and toxicity.

In addition, the real-world examples are included in the review that pharmacogenomic testing for high-risk drugs, aminoglycosides, anticonvulsants, and opioids is feasible, has clinical value, and is cost-effective in the NICU setting. Several challenges of ethical consent, lack of neonatal-specific databases, delayed test results, and gaps in provider education stand in the way of its successful clinical application in this population. Practical tools for integration include the advances on next-generation sequencing, point of care genotyping, as well as AI-powered decision support systems. The evolution of neonatal-specific frameworks, the adoption of genome-informed care by health systems, will lead to the use of genome-based precision dosing that will lead to ultimately reduce dose-related adverse drug reactions and advance health outcomes in neonates. This review demonstrates that it is feasible and necessary to tailor neonatal drug therapy according to the genetic profile to usher in a new era of safe, effective, and customized medicine in neonatal care.

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