Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 1s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Investigating the role of pharmacogenomics in optimizing pediatric medication therapy: a pilot study

Smruti Ranjan Dash[1], Mahendra Kumar Sahu[2]

[1]Assistant Professor, Department of Pharmacy, Kalinga University, Raipur, India.
[2]Research Scholar, Department of Pharmacy, Kalinga University, Raipur, India.

Cite this paper as: Smruti Ranjan Dash, Mahendra Kumar Sahu, (2025) Investigating the Role of Pharmacogenomics in Optimizing Pediatric Medication Therapy: A Pilot Study. *Journal of Neonatal Surgery*, 14 (1s), 79-87.

ABSTRACT

The Food and Medication Organization and the Public Establishments of Wellbeing have worked to move pharmacogenomics from the laboratory to the patient's bedside. Pharmacogenomic data is now included on the label of more than 100 pharmaceutical drugs. In the pediatric population, several of these are often utilized. Additionally, medical practitioners must intervene and provide advice regarding direct-to-consumer genetic test kits. Healthcare workers must gain a basic understanding of pharmacogenomics and how it applies to patient care in light of the growing trend toward customized treatment. Because pharmacogenomic testing can provide patient-explicit indicators for medication reaction and security, pharmacologists can effectively participate in clinical understanding of results, pharmacogenomic testing, and ideas for individualizing drug treatment. In both short-term and long-term contexts, drug specialists can identify possible opportunities, such as demonstrating pharmacogenomic testing to patients and their families and supervising the implementation of clinical pharmacogenomics meetings. Pharmacists may work in clinical settings as well as in medication development and discovery that is impacted by genetics. The creation of interprofessional practice guidelines and dosing recommendations for pharmacogenomic testing in pediatric patients should involve pediatric pharmacists because of the possibility that age-dependent and genetic factors would affect drug selection and dosage. The purpose of this pilot project is to investigate how pharmacogenomics can be used to customize prescription regimens for young patients in order to increase effectiveness and lower adverse drug reactions (ADRs).

Keywords: *Pharmacogenomics, pediatric, drug therapy*

1. INTRODUCTION

Adverse effects are frequently unforeseen, and patient response to medication therapy varies greatly. While some people may need a significantly higher dose of a given medication to obtain a comparable therapeutic response, others may experience severe adverse effects to very modest doses of the same medication. The application of pharmacogenomic testing in understanding consideration is also being aided by the growing availability of genetic tests in clinical labs and the decline in scientific costs. The dedication to "customized medication" is developing at such a slow rate. Hereditary traits will undoubtedly play a big role in medication discovery, development, and treatment sooner rather than later. Genomics is also becoming a powerful clinical tool for drug specialists when utilized to create customized treatment strategies for individual patients. This could finally address the possibility of selecting the best medication at the proper dosage for the correct comprehension or possibly reducing the frequency of antagonistic pharmaceutical events. Despite the educational program for drug store schools, PPAG supports the creation of center capabilities or maybe certificate courses to guarantee that drug specialists have a solid understanding of pharmacogenomics and are equipped to handle changed pharmacotherapy.[1] Furthermore, according to PPAG, using pharmacogenomics in children presents unique ethical, interpretative, and specialized challenges that call for data on drug specialists who have had pediatric-specific training. The purpose of this method pronouncement is to explicitly support PPAG's belief that pediatric drug experts are essential for the clinical translation and application of pharmacogenomic testing in pediatric pharmacotherapy. It explains why pediatric drug specialists should be involved with pharmacogenomics, highlights the possible roles that pediatric drug specialists could play, and provides guidance on how drug specialists should get ready to integrate pharmacogenomics into their clinical practice. High-throughput genomic breakthroughs have improved our understanding of the pathophysiology of illness and enabled more accurate depictions of poisonousness and restorative reactions based on an individual's genetic makeup [9].

Pharmacogenomics is a valid technique for determining who is more likely to respond to therapy or who is at a high risk of suffering from severe adverse medication reactions. Although pharmacogenomic studies are increasingly being conducted, most of them only include adults.[2].

Research question

How can pediatric patients' medication therapy be optimized using pharmacogenomics to increase therapeutic efficacy and reduce adverse drug reactions?

1.1 Objectives

- To assess if using pharmacogenomic testing in pediatric clinical settings is feasible.
- To evaluate how PGx-guided therapy affects the safety and effectiveness of medications.
- To determine which frequent genetic variations in a juvenile population are linked to medication response.

2. LITERATURE REVIEW

Enhancing a pharmacological therapy's efficacy or safety, or both, is the goal of a pharmacogenomic test. This is accomplished by using pharmacogenetic data, or the parts of a patient's genetic composition that are pertinent to medicine therapy, to guide prescription decision-making [3]. Even though the degree of hereditarily determined fluctuation in drug reaction may vary greatly, the genetic information obtained from a PGx test should be a reliable indication of medication reaction to be deemed relevant to clinical practice. Hereditary characteristics of complex illnesses include a few significant traits (such as schizophrenia, type 2 diabetes, and hypertension), each of which has a slight impact on the others. However, from a developmental perspective, the body's susceptibility to medications is a unique characteristic, and evidence suggests that genetic differences influencing drugs typically have larger impact sizes, indicating their possible clinical relevance. Findings from a PGx test can distinguish between drug responders and non-responders, reveal a genetic predisposition to an adverse drug reaction (ADR), or show that a different medicine class or dosage is required. Results that might significantly alter the patient's advantage to harm ratio and influence the prescriber's choices are considered noteworthy PGx results. PGx testing might be responsive or preplanned. When a drug is regulated in relation to a known pharmacogene—the characteristic that is pertinent to the clinical pharmacology of that particular substance—responsive testing takes place at or close to that remedy time. This step should be completed as soon as possible to ensure that the results are available and can be used to identify the genuine drug.[4] Although the rationale for PGX testing is essentially the same for adults and children, the relevant ideas are presented here from a pediatric perspective. If a child has an actionable PGx result, a pediatrician (or a physician treating the same patient in adulthood) should make alternative options when administering the right prescription or medications. Thus, PGx material needs to be easily readable and available in compliance with the latest evidence-based pediatric PGx guidelines. It is accurate to say that not all children will immediately benefit from PGx, and not all prescriptions will either. This does not, however, mean that children who need it should not have proper PGx testing as part of their routine care.

Furthermore, all prescribers should have access to this information in order to avoid unnecessary test repetition, which could put the child in risk and result in additional costs. It shouldn't matter if the prescribing clinician ordered the test or even if they work at the same institution. Despite the need for improved PGx proof in children, a major obstacle at the time was the lack of well defined pediatric PGx recommendations and efficiently available PGx testing.[11] This necessitates expanding the usage of recently approved testing techniques for standard use in medical services frameworks, which can be difficult. Compared to adult medication, research investigations and implementation strategies to update drug marking and evidence-based regulations in pediatric pharmacology have typically been delayed. This delay typically stems from a variety of factors, such as financial, ethical, and strategic barriers to pediatric research, many of which are now mostly past due to concerted global efforts to accelerate the development of pediatric drugs. Aronson and associates.[5]. Recently, it has been discovered that a potentially related problem, when combined with an excessive focus on clinical review and initial results, may be the cause of the present delays in PGx organization. The phrase "unthinking proof" refers to any type of evidence supporting the existence or specifics of a certain pharmacological system, including in vitro, ex vivo, clinical, observational, and recreational studies.

3. METHODOLOGY

- **Study design:** pilot study employing a prospective observation technique.
- **Setting:** establishments with pharmacogenomic testing capabilities, including pediatric healthcare facilities or hospitals.

Inclusion criteria: Children between the ages of 1 and 18 who are prescribed drugs with established pharmacogenomic markers satisfy the inclusion requirements.

Exclusion criteria: Individuals with insufficient medical data or those who are not suitable candidates for genetic testing

are excluded.

Intervention: Pharmacogenomic testing of important genes, such as CYP2D6, CYP2C19, TPMT, and VKORC1, involved in drug metabolism and response is part of the intervention. When necessary, treatment strategies are modified based on pharmacogenomic data.

Data collection: For this study, clinical and genetic data will be collected from pediatric patients. Baseline pharmacogenomic testing will be performed to identify genetic variants associated with medication metabolism and response, with a focus on genes such as CYP2D6, CYP2C19, TPMT, and VKORC1. Clinical data, including prescription regimens, dosages, and indications, will be documented at the time of enrollment. Participants will be monitored for six to twelve months, during which time adverse drug reactions (ADRs) and treatment results will be recorded. Additional data on patient demographics, medical history, and co-administered medications will be collected in order to account for confounding variables. Formal questionnaires will be utilized to document healthcare practitioners' perspectives on the value of pharmacogenomic data, and surveys or interviews will be used to get caregiver input on medication results and satisfaction. All data will be anonymized and securely kept to preserve participant confidentiality.

3.1 Assessing PGx evidence

Many of the available PGx proof has been investigated and compiled by master PGx consortia, including data from numerous previous RCTs in (mostly adult) patients that demonstrated the therapeutic benefit of PGx testing.

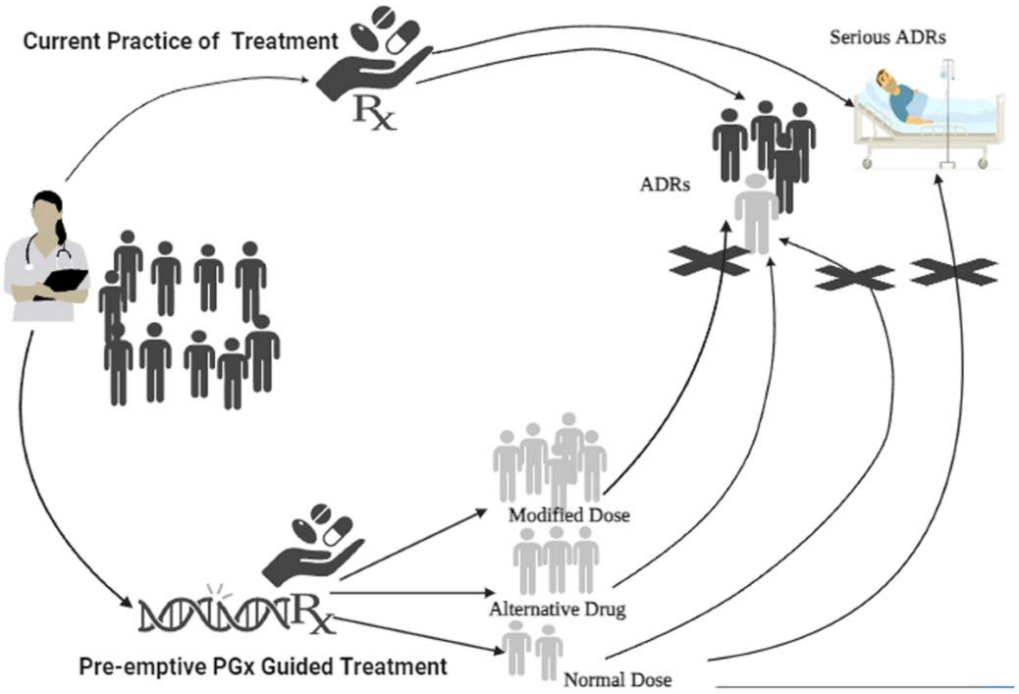


Figure 1: Assessing PGx evidence

Incorporating and dissecting the accumulated data from PGx research, including children, will be essential as execution efforts proceed, necessitating an evaluation of the quantity and kind of available evidence. It would be futile, irrational, and exploitative to demand unquestionable pediatric (or adult) RCTs to assess the restorative meaning of each and every PGx quality/drug combination [16]. Additionally, it disregards the possible advantages of using cutting edge sequencing (NGS)-based methods like the PGx board. Similar to how medication portion recommendations are regularly modified for patients with renal or hepatic brokenness, where necessary, without specific preliminary testing in these particular populations, it would seem legitimate to move toward PGx data (using data from either drug improvement or post-showcasing studies) based on sound pharmacological standards. This would entail prescribing medications appropriately based on the provided PGx results. [6].

3.2 Implementing PGx testing in pediatrics: strategies and challenges

The challenging process of integrating logical knowledge into medical services strategy and practice is being significantly altered by the rapidly evolving field of execution science [13]. Despite the evaluations of various partners, anticipated benefits, unexpected consequences, and expenses, medical services chiefs, directors, and PGx specialists should take the aforementioned concerns into account while developing a pediatric PGx strategy. It will be necessary to carefully coordinate institutional, provincial, and public execution strategies in order to incorporate PGx standards into routine clinical

practice.[7]. The best components of these drives are CDs innovations that are offered in relation to a specific PGx counseling administration and fully integrated into the electronic wellbeing record (HER). Three pediatric clinics in the United States began participating in the Electronic Clinical Records and Genomics (Arise) Organization's Stage II, which includes a comprehensive PGx execution study, in August 2012.[14]. This demonstrates that PGx consortia's efforts to create PGx practice guidelines and the tactics employed for adult patients are not always separate from concepts addressing the needs and implementation strategies of pediatric PGx.[12]. It is recommended that when planning the implementation of pediatric PGx in various countries, consideration be given to the evidence, insight, and execution science. [18]. The program's structure should be continuously assessed for clinically meaningful results, looking at predicted success and cost-effectiveness indicators. With the decline in the cost of hereditary testing, PGx testing has become more accessible and affordable. [8].

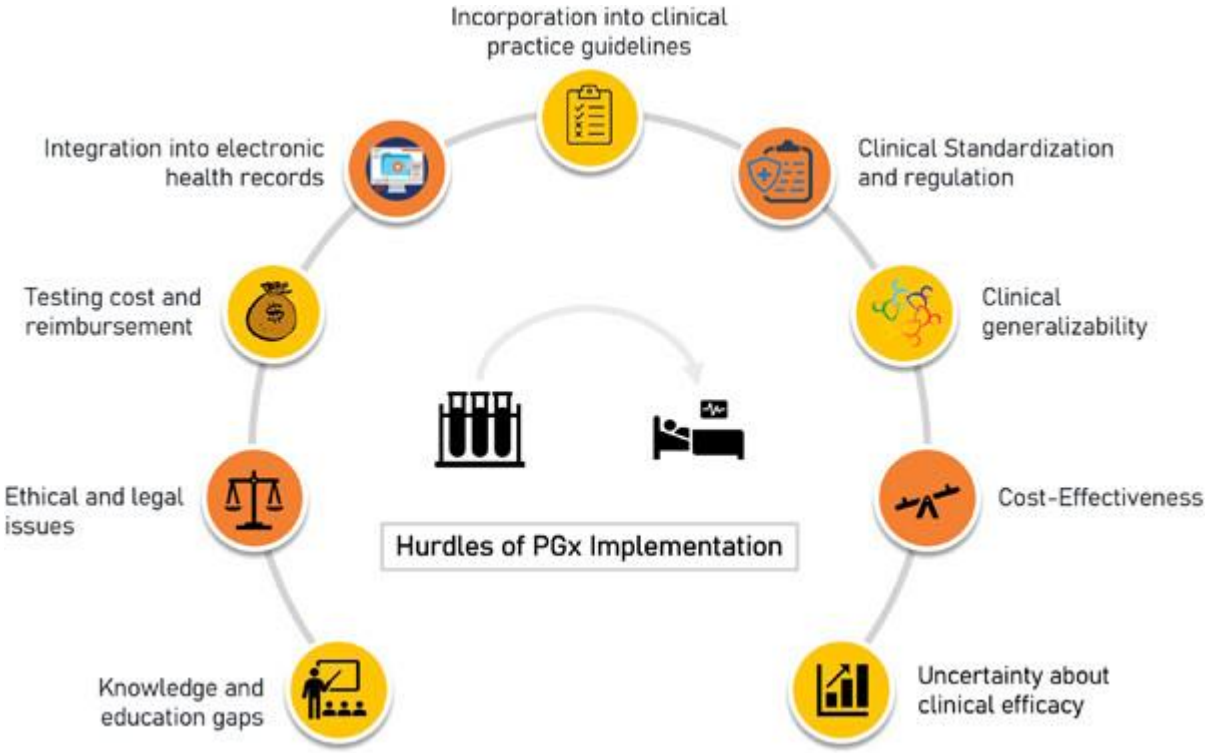


Figure 2: Approaches and hurdles of implementing pharmacogenetic testing in the pediatric clinic

4. EXPECTED OUTCOME

One of the most crucial medications for the prevention and treatment of tuberculosis is isoniazid (INH). Since isoniazid has been used to treat tuberculosis for more than 50 years, resistance has developed, making isoniazid (INH) resistance more common and significantly higher than RIF (WHO 2014). Mono-resistance against INH affects 10–19% of TB patients worldwide and 9–18% of TB patients in India (Agarwal and Chauhan 2005). Each patient metabolizes INH in a unique way. INH loses its therapeutic activity when N-acetyltransferase acetylates it to acetylisoniazid. The current regimen is intended to prevent the hazardous side effects that slow acetylators are more likely to experience. None of the many metabolites of INH are effective against tuberculosis, despite their differing levels of toxicity and elimination curves. The host's and M. tuberculosis's metabolic pathways for INH and its metabolites are not well understood. We may be able to rationalize therapy at the individual level if we can properly and affordably detect the genetic polymorphisms of N-acetyltransferases, which are the primary basis for the varying pharmacologic profile of INH.[17].

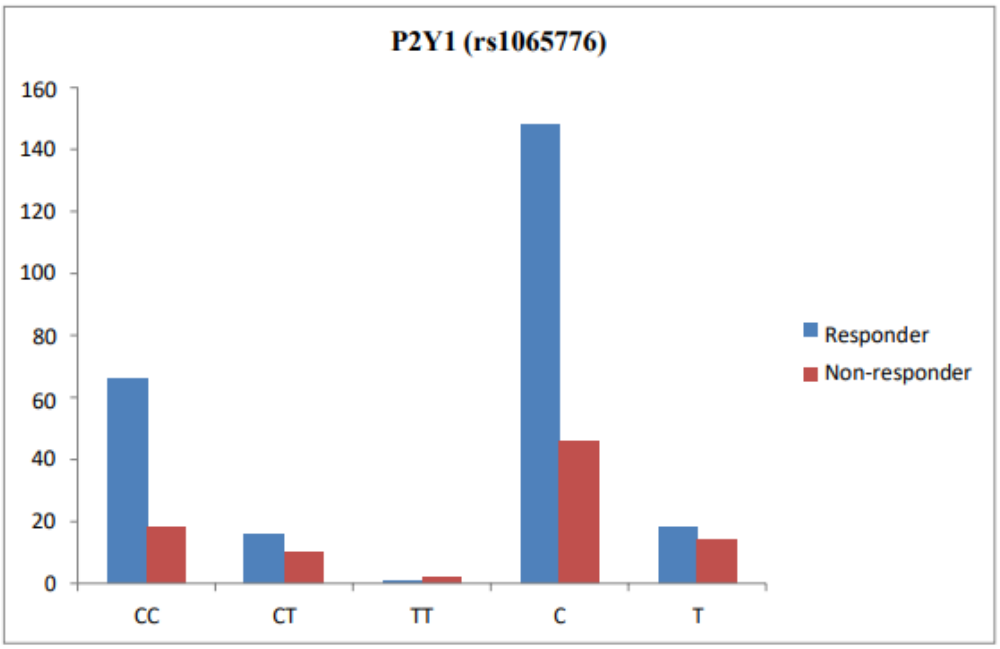


Figure 3: Graphical representation of P2Y1 (rs1065776) genotypes and allelic frequencies among (0-5 years)

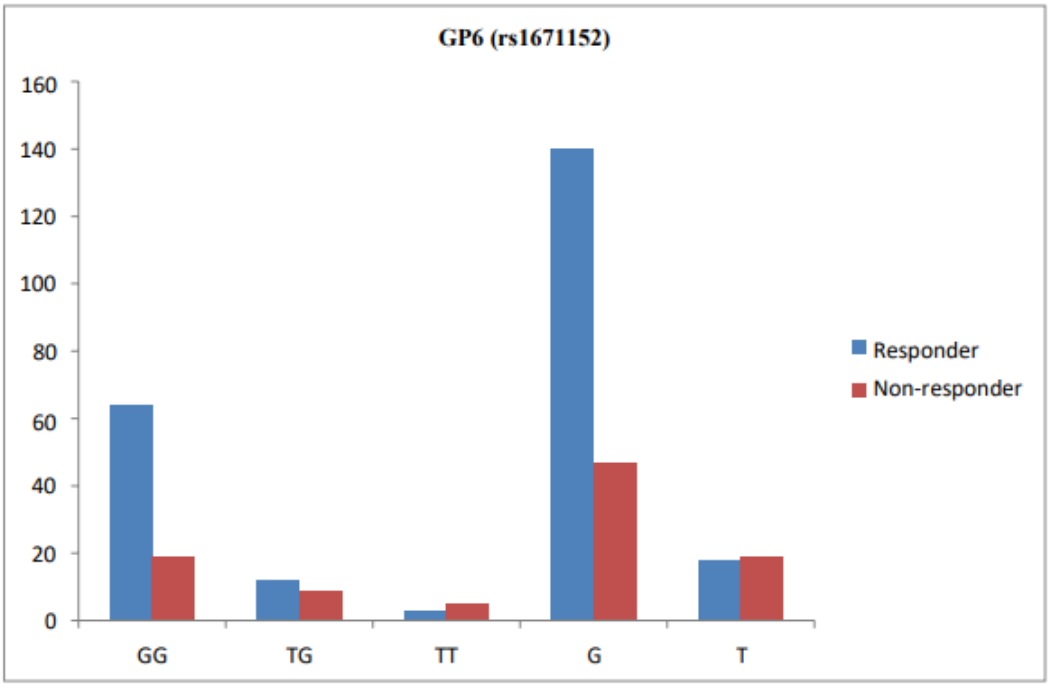


Figure 4: Graphical representation of GP6 (rs1671152) genotypes and allelic frequencies among (5-10 years)

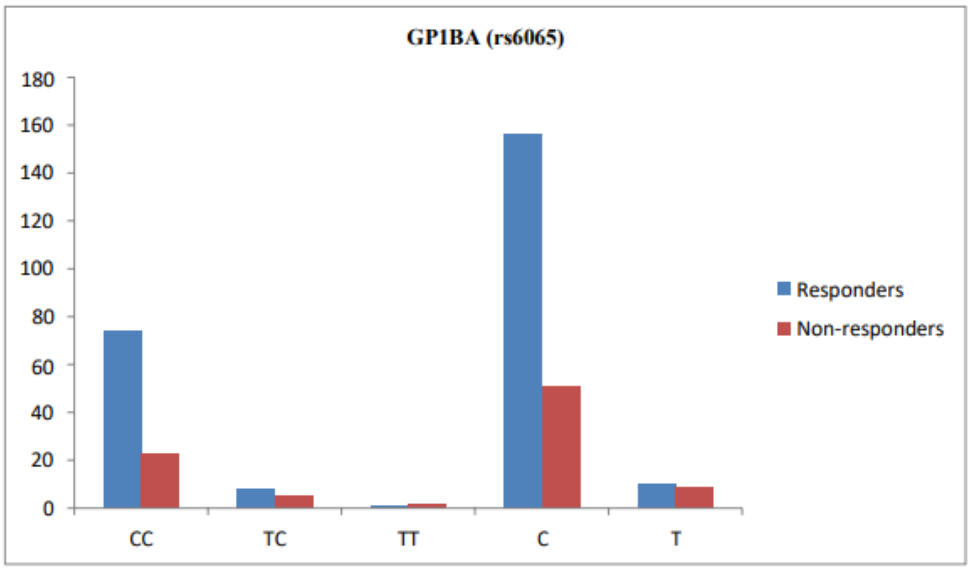


Figure 5: Graphical representation of GP1BA (rs6065) genotypes and allelic frequencies among (11-18 years)

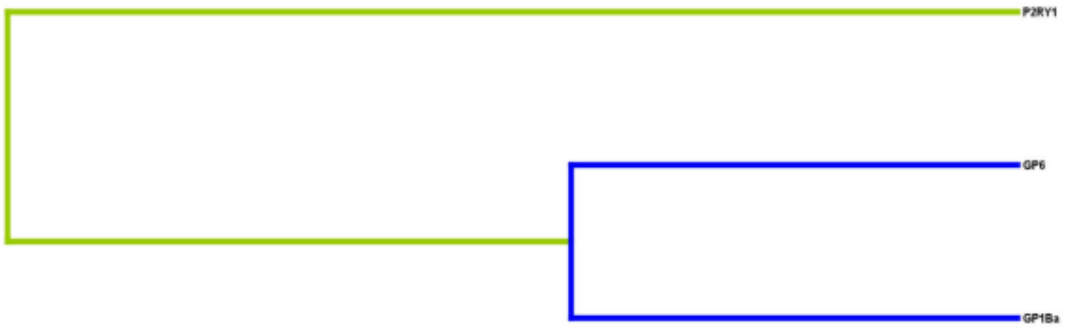
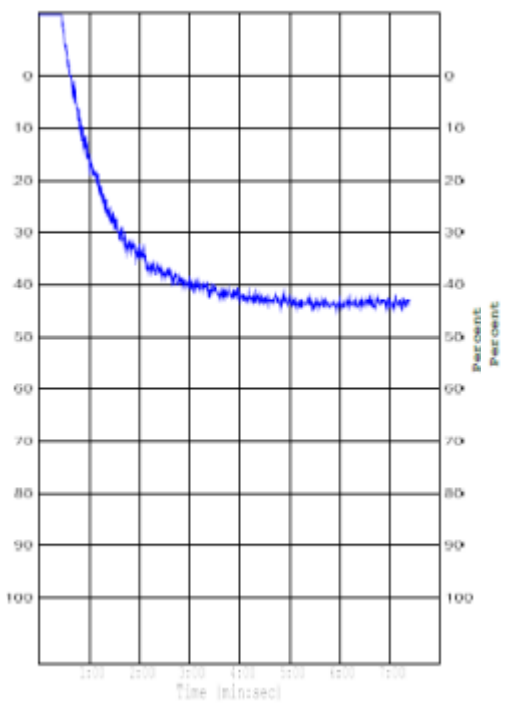
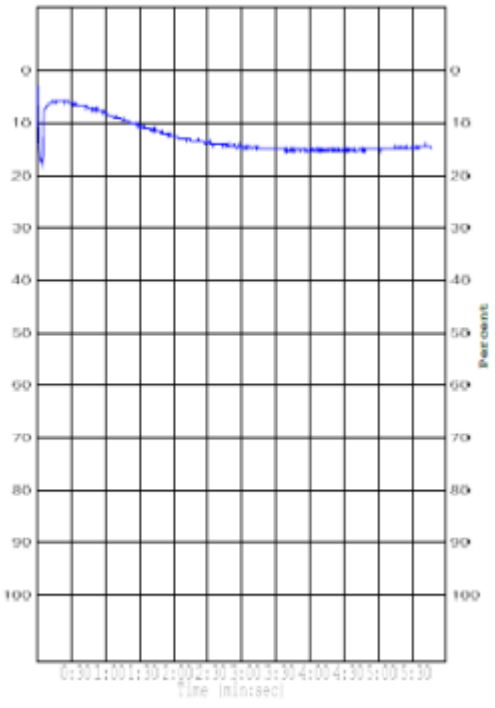


Figure 6: Gene-gene interaction dendogram

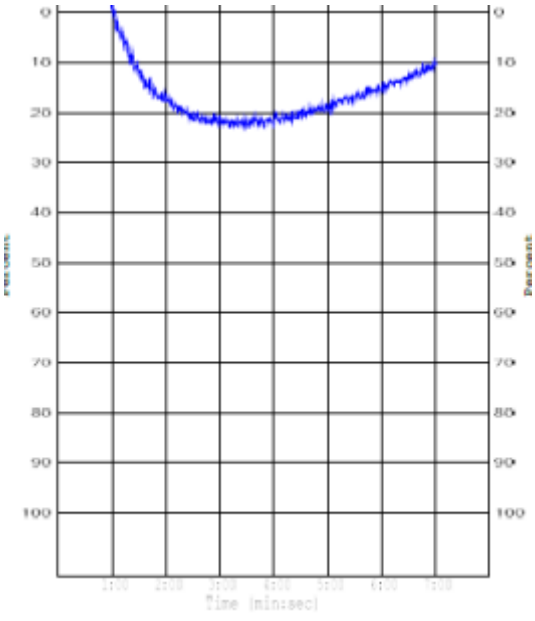
Multifactor dimensionality reduction, or MDR, is a computational method for detecting complex gene-gene and gene-environment interactions. A data reduction technique is used to find multi-locus genotype combinations that represent sickness risk in complex conditions. MDR reduces data to a single dimension by pooling genes into response or non-response groups. The longitudinal bars' positions show how strong the dependency is; a blue bar denotes a positive interaction, while a green bar denotes a weaker link. Genes with missense mutations (GP6 and GP1BA) were grouped together by the hierarchical cluster evaluation, indicating a substantial interaction between these SNPs. In contrast, P2RY1 displayed a lesser correlation (Fig. 6). ADP-induced platelet aggregation in citrated PRP from 19 ischemic stroke patients was assessed using the light transmittance test (LTA) with a 4-channel platelet aggregometer that was continuously stirred at 1200 rpm and 37º Celsius.[10]. Based on their clinical results, the 19 ischemic stroke patients were categorized as either responders or non-responders. Two patients had poor clinical outcomes, whereas 17 of the 19 patients had excellent clinical outcomes based on the mRS score. After baseline calibration, ADP was injected at a final concentration of 5 µ M, and aggregation was monitored for six minutes. The greatest aggregation (%) during the first six minutes following the injection of ADP was the parameter under analysis. The agonist caused the platelets to aggregate into ever-larger clusters and the PRP to start clearing, which allowed more light to pass through. Light transmittance increases in direct proportion to the amount of aggregation.[15].



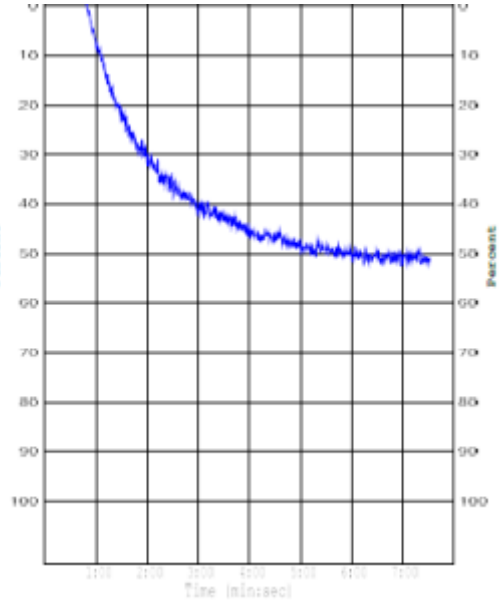
Plot showing 43% platelet aggregation



Plot showing 15% platelet aggregation



Plot showing 10% platelet aggregation



Plot showing 50% platelet aggregation

Figure 7: Aggregation plot

Gene expression clustering makes it possible to explore the data in an open-ended manner without becoming bogged down in the thousands of distinct genes. Gene clusters have several significant computational uses in addition to basic visualization. To identify cis-administrative regions in the advertisers of firmly coexpressed characteristics, for example, Tavazoie et al. used bunching. It may be useful to include obscure attributes within a same group, as quality articulation bunches are often notably strengthened for explicit utilitarian classifications.A dendrogram, or tree-molded information structure, is produced in different tiered bunching by further splitting each group into smaller groupings. Similarly used in phylogenetics, agglomerative various levels bunching starts with the single-quality groups and unites the closest groups one after the other until every quality is necessary for the supercluster. The primary difference between a whole set of bunching techniques is actually the meaning of the "linkage capability," often known as the intercluster distance. The most widely used ones are centroid linkage/UPGMC (unweighted pair-bunch technique using centroids; distance between the group centroids), normal

linkage/UPGMA (unweighted pair-bunch strategy using number-crunching midpoints; normal distance between any two individuals), single linkage (the distance between bunches is the briefest distance between any two individuals from the bunch), and complete linkage (biggest distance between any two individuals).

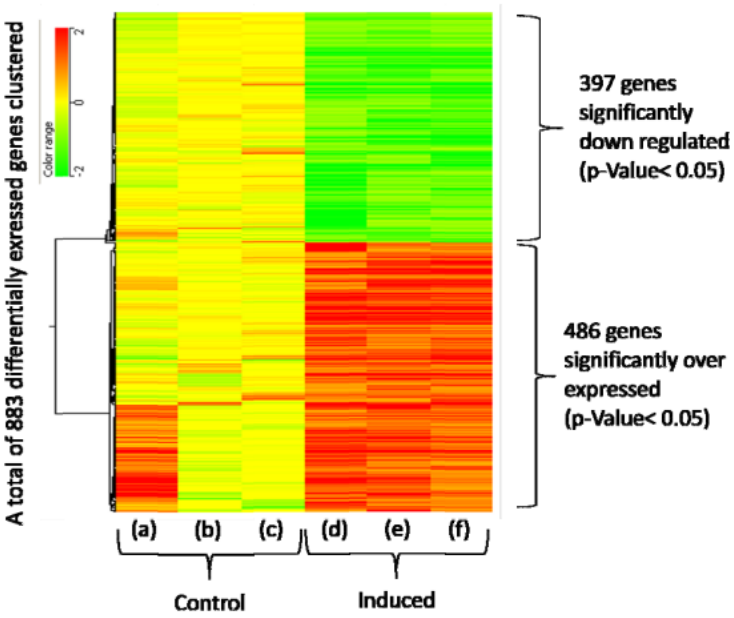


Figure 8: gene clustersring

Thus, the current study's findings show how genetic variations and the safety and effectiveness of medications in pediatric patients are related, which lays the groundwork for the application of pharmacogenomics to tailor medication therapy and enhance children's health outcomes.

5. CONCLUSION

Children are entitled to the advantages of genomic medicine, including PGx-informed treatments that are supported by substantial evidence and can be implemented at a reasonable cost. When implementing novel pediatric pharmacogenomic testing techniques in any intricate healthcare system, numerous obstacles are unavoidable. With the support of globally funded pediatric research institutions, the collaborative efforts of the pharmacogenomic local area will continue to bring PGx benefits to the bedside as the genomic pharmaceutical insurgency begins. Maintaining an active dialogue with the pediatric workforce is essential to ensuring that children have further developed access to pharmacogenomic testing in a reasonable, evidence-based, and conservative manner. Practically speaking, the ultimate goal of proof-based PGx is to provide pediatric prescribers with timely and reasonable PGx results, supported by top-notch genomic training resources and continuously informed by a cycle of improvement that takes partner input, review results, and the most recent examination discoveries into account. To help construct globally understood PGx norms, it will also be crucial for administrative offices and PGx consortia to cooperate on appropriate pediatric ideas.

REFERENCES

[1] Maagdenberg H, Vijverberg SJ, Bierings MB, Carleton BC, Arets HG, de Boer A, Maitland-van der Zee AH. Pharmacogenomics in pediatric patients: towards personalized medicine. Pediatric Drugs. 2016 Aug;18:251-60.

[2] Yadav S, Uraon A, Kumar Sinha M. Evaluating awareness and usage of library services among undergraduate students of Silchar Medical College, Silchar, Assam. Indian J. Inf. Sourc. Serv. 2019;9(1):25-9. https://doi.org/10.51983/ijiss.2019.9.1.601

[3] Rollinson V, Turner RM, Pirmohamed M. Pharmacogenomics: an overview. Clin Pharm. 2017;9(10).

[4] Maranville JC, Cox NJ. Pharmacogenomic variants have larger effect sizes than genetic variants associated with other dichotomous complex traits. The pharmacogenomics journal. 2016 Aug;16(4):388-92.

[5] Sathyanarayanan S, Srikanta MK. Heart sound analysis using SAINet incorporating CNN and transfer learning for detecting heart diseases. Journal of Wireless Mobile Networks, Ubiquitous Computing, and Dependable Applications (JoWUA). 2024;15(2):152-69. https://doi.org/10.58346/JOWUA.2024.I2.011

[6] Mansour R. A conceptual framework for team personality layout, operational, and visionary management in online teams. Global Perspectives in Management. 2024;2(4):1-7.

[7] Carvalho AA, Karthikeyan K, Sudhahar JC, Jesiah S. Risk assessment and decision-making in geology-driven projects: a management perspective. Archives for Technical Sciences. 2024 Dec 24;2(31):329-39. https://doi.org/10.70102/afts.2024.1631.329

[8] Turan F, Ergenler A, Bardakcı F. Monitoring DNA Damage in Suez Pufferfish (Lagocephalus suezensis) from the Northeastern Mediterranean. Natural and Engineering Sciences. 2022 Aug 1;7(2):190-9. http://doi.org/10.28978/nesciences.1159286

[9] Stevens A, De Leonibus C, Hanson D, Whatmore A, Murray P, Donn R, Meyer S, Chatelain P, Clayton P. Pediatric perspective on pharmacogenomics. Pharmacogenomics. 2013 Nov 1;14(15):1889-905.

[10] Menon PA, Gunasundari R. Deep Feature Extraction and Classification of Alzheimer's Disease: A Novel Fusion of Vision Transformer-DenseNet Approach with Visualization. https://doi.org/10.58346/JISIS.2024.I4.029

[11] Aronson JK. Adjusting therapeutic dosage regimens to optimise the balance of benefit to harm. Clinical medicine. 2005 Jan 1;5(1):16.

[12] Khodjaev N, Boymuradov S, Jalolova S, Zhaparkulov A, Dostova S, Muhammadiyev F, Abdullayeva C, Zokirov K. Assessing the effectiveness of aquatic education program in promoting environmental awareness among school children. International Journal of Aquatic Research and Environmental Studies. 2024;4(Supplement 1):33-38.. https://doi.org/10.70102/IJARES/V4S1/6

[13] Wensing M, Grol R. Knowledge translation in health: how implementation science could contribute more. BMC medicine. 2019 Dec;17:1-6.

[14] Kabirian M, Sardari D, Babapour F. Determination of proper neutron beam energy spectrum for penetration depth in liver BNCT. International Academic Journal of Science and Engineering. 2016;3:106-14. Retrieved from https://iaiest.com/iaj/index.php/IAJSE/article/view/IAJSE1410019

[15] Shrivastav P, Malakar U. Exploring Barriers to Medication Adherence Among Patients with Chronic Diseases. Clinical Journal for Medicine, Health and Pharmacy. 2024 Sep 30;2(3):21-31.

[16] Gammal RS, Caudle KE, Klein TE, Relling MV. Considerations for pharmacogenomic testing in a health system. Genetics in Medicine. 2019 Aug;21(8):1886-7.

[17] Hemmati M, Mehrabi AM, Karamkhani J, Haidari Z, Poor HRS, Moradi A, Ranjbari M. Studying and comparing the effectiveness of brain stimulation over the skull through TDCS direct electrical current and matrix to reduce craving of methamphetamine. International Academic Journal of Social Sciences. 2014;1(2):71–79. Retrieved from https://iaiest.com/iaj/index.php/IAJSS/article/view/IAJSS1410019

[18] Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. The lancet. 2003 Oct 11;362(9391):1225-30.