A review on Parmacogenomics

Pawar Shivkanya[1], Nirmala Musmade[2]
[1]*Student, Yashodeep Institute of Pharmacy*
[2]*Assistant.Professor, Yashodeep Institute of Pharmacy*

***Abstract*—Pharmacogenomics is the study of how a person's genes affect the way their body responds to medicines. It is a growing area of science that combines pharmacology, which focuses on drugs and their actions, with genomics, which deals with the study of genes. The aim of pharmacogenomics is to make medical treatment safer and more effective by selecting the right drug and the correct dose for each individual based on their genetic makeup. By examining genetic variations across the entire genome, pharmacogenomics helps explain why people respond differently to the same medication.To support the use of pharmacogenomics in healthcare, many tools and resources have been developed to help researchers, doctors, and patients better understand its benefits. In clinical practice, common genetic variations can influence how drugs work in the body, and pharmacogenomics can be used to guide personalized treatment decisions. The application of pharmacogenomics allows healthcare professionals to choose appropriate medicines and adjust doses more accurately. This personalized approach can improve treatment outcomes, reduce harmful drug reactions, lower the risk of illness and death related to medications, and offer a cost-effective way to deliver patient care.**

***Index Terms*—Pharmacogenomics, clinical implementation, personalized madicine,breast cancer.**

I. INTRODUCTION

Pharmacogenomics is the field of science that studies how differences in a person's genes affect the way they respond to medicines. Although the terms pharmacogenetics and pharmacogenomics are often used interchangeably, they are slightly different. The idea that genetics can influence drug response dates back to the 1930s, when researchers first noticed that natural variations in enzymes could change how individuals reacted to certain drugs. Later, in 1959, the German scientist Friedrich Vogel introduced the term pharmacogenetics to explain how the effect of a drug could be influenced by a single gene (1-4). Pharmacogenomics applies modern genomic tools to understand how drugs act in the body, how they are distributed, and how they produce their effects. This approach helps explain why the same drug may be effective for one patient but ineffective or harmful for another. Such knowledge forms the foundation of personalized medicine, where treatments are designed according to the genetic characteristics of each patient. More recently, the concept of stratified medicine has been introduced to describe the use of genetic information to classify patients into groups with similar drug responses rather than focusing on individuals alone (5).

Rapid advances in technology and a significant reduction in the cost of genetic testing have made techniques such as exome sequencing more accessible. These tools are now widely used in research, particularly for identifying genes linked to rare diseases. Pharmacogenomics has also found practical applications in clinical treatments, including cancer chemotherapy and the use of oral anticoagulants. By using information about a patient's genetic profile, clinicians can choose the most suitable drug and dose, thereby reduce side effects and prevent treatment failure. As a result, traditional trial-and-error approaches to drug selection are increasingly being replaced by pharmacogenomic-based strategies (6).

Research has identified many genetic variations that influence how drugs are absorbed, distributed, metabolized, and eliminated from the body, as well as how they produce their therapeutic effects. Patients carrying certain genetic variants may be at a higher risk of experiencing severe or even life-threatening adverse drug reactions. These reactions are a major cause of illness and death and also create a significant economic burden on healthcare systems. Importantly, studies suggest that nearly half of these adverse drug

reactions could be prevented through the effective use of pharmacogenomic information

What Is Pharmacogenomics?

Pharmacogenomics is a broad scientific concept that focuses on using genetic information to improve how medicines are discovered, developed, and used. At its core, pharmacogenomics aims to move away from a "one-size-fits-all" approach to treatment and instead develop medicines that are better suited to specific groups of people or individual patients. This approach is commonly known as personalized medicine, which combines insights from functional genomics and molecular pharmacology to create more precise and effective therapies.(7).

The main goal of pharmacogenomics Is to understand the connection between a patient's genetic makeup and their response to treatment. By studying these genetic differences, scientists can identify why certain drugs are highly effective for some individuals while providing little benefit or causing side effects in others. This knowledge allows researchers to design therapies that are specifically tailored to particular genetic profiles, leading to improved treatment outcomes (8). Pharmacogenomics involves identifying genes and the proteins they produce as potential targets for new drugs and then studying how variations in these genes affect drug response. Growing scientific evidence shows that an individual's genetic profile is one of the most important factors in predicting how well a therapy will work. Because of this strong link between genetics and treatment success, interest and investment in pharmacogenomics continue to increase, highlighting its importance in the future of personalized healthcare (9).

Principle of Pharmacogenomics

Genetic Basis of Differences in Drug Response Doctors often notice that patients can react very differently to the same medicine, even when they receive the same dose. One major reason for this difference is genetics. Variations in genes that control drug-metabolizing enzymes, drug transporters, drug targets, and drug receptors—commonly called pharmacogenes—can change how these proteins work or how much of them the body produces. These changes can affect how a drug is absorbed, broken down, distributed, and removed from the body, as well as how strongly it works.Certain genetic differences, especially in genes related to human leukocyte antigens (HLAs), can increase a person's risk of developing immune-related allergic reactions to specific medicines. Some of these reactions can be serious or even life-threatening. Because of this, genetic information can serve as a valuable tool to help healthcare professionals choose the safest medicine and the most appropriate dose for each individual patient. Many important pharmacogenomic examples involve genes that control how drugs are broken down in the body, especially the cytochrome P450 (CYP) enzymes. Because of genetic differences, people process medicines at different speeds. Some people break down drugs very fast, while others do it slowly. If a medicine is already active and the body's enzymes change it into an inactive form, fast drug breakdown can reduce the drug's effect and cause treatment failure. In contrast, slow drug breakdown can cause the drug to stay in the body longer, increasing the risk of side effects or toxicity.

For medicines called prodrugs, which must be changed into an active form to work, the opposite happens. People who process drugs quickly may experience stronger effects or side effects, while those who process drugs slowly may not get enough benefit from the medicine.Whether these genetic differences cause problems in real-life treatment depends on several factors, such as how sensitive the drug is to dose changes and whether the body has other ways to break down the drug.

History

The foundation of genomics was laid by Fred Sanger, who was the first to sequence the complete genomes of a virus and a mitochondrion. His work led to the development of key techniques such as DNA sequencing, genome mapping, data storage, and bioinformatic analysis during the 1970s and 1980s. The term genomics is believed to have been introduced in 1986 by Dr. Tom Roderick, a geneticist at the Jackson Laboratory in the United States, during an informal discussion at a meeting focused on mapping the human genome. (10). Pharmacogenomics has the potential to significantly lower healthcare costs by reducing the number of adverse drug reactions and failed clinical trials. It can also shorten the time

required for drug approval, reduce how long patients need to stay on medications, and decrease the number of drugs a patient must try before finding an effective treatment. Additionally, early and accurate diagnosis through pharmacogenomics can reduce the overall impact of disease on the body.(11)

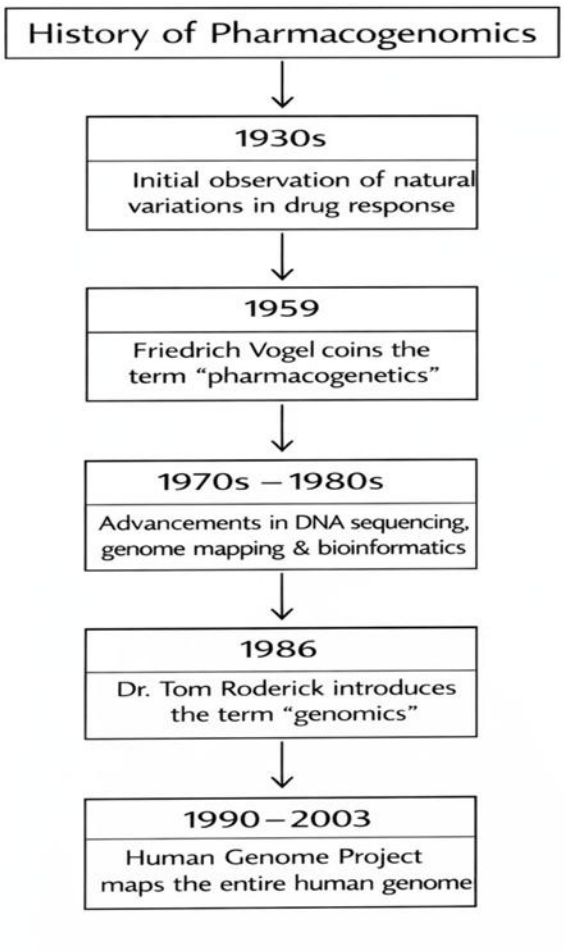

Fig 1 : History of Pharmacogenomics

Importance of Pharmacogenomics

The main aim of pharmacogenomics is to use genetic information to improve drug therapy by increasing drug effectiveness and reducing unwanted side effects. To support this goal, several pharmacogenetic tests have been developed that help guide both diagnosis and treatment decisions. These DNA-based tests detect genetic variations that may increase the risk of adverse drug reactions or poor treatment response. Many important pharmacogenetic tests have been available for years in laboratories approved under the Clinical Laboratory Improvement Amendments (CLIA). However, their use in routine clinical practice is still limited. Regulatory authorities such as the U.S. Food and Drug Administration (FDA) recognize specific genetic variants, known as pharmacogenetic biomarkers, that influence how well a drug works and how safe it is.(12).

The main goal of pharmacogenomics is to use a person's genetic information to choose the right medicine and the right dose. This helps make drug treatment more effective and reduces the chances of harmful side effects. Because of this benefit, many pharmacogenetic tests have been developed and are now helpful in both diagnosis and treatment planning. Pharmacogenomic testing is a DNA-based test that detects genetic changes that may affect how a person responds to a medicine or whether they are at risk of side effects. Although several important pharmacogenetic tests have been available for many years in Clinical Laboratory Improvement Amendments (CLIA)–approved laboratories, their use in routine clinical practice is still limited.

The Food and Drug Administration (FDA) identifies specific genetic variations, known as pharmacogenetic biomarkers, that influence how well a drug works and how safe it is. These biomarkers support the development and selection of medicines that benefit many patients. However, there is no single drug that works equally well for everyone, and this can sometimes lead to serious treatment problems(13)

Pharmacogenomics and Drug Development

In the past, drug discovery—especially in psychiatry—often occurred by chance. Drugs such as lithium and chlorpromazine were found to be effective before their exact mechanisms of action were fully understood. Modern drug development now follows a more structured approach, using techniques like combinatorial chemistry and biological screening to identify compounds that interact with specific receptors or biological targets.Pharmacogenomics builds on research methods from population genetics and earlier genetic studies of complex diseases. The Human Genome Project revealed that nearly all human genes could serve as potential drug targets. One of the major challenges in drug development is understanding how these genes and the proteins they produce can be used effectively for treatment.

Technological advances, particularly DNA microarrays, have played a crucial role in pharmacogenomic research. Microarrays allow scientists to examine gene expression patterns and genetic variations across the entire genome. In this technique, thousands of DNA fragments are fixed onto a solid surface such as glass or silicon. Each fragment represents a specific gene or genetic sequence, enabling the detection of genetic variations or changes in gene activity through hybridization and fluorescence-based methods(14)

Pharmacogenomics in the Era of Next-Generation Sequencing: From Data to Bedside(15)

Thanks to advances in sequencing technology, pharmacogenomics is now moving from laboratory research to practical patient care. In blood cancers, survival rates for both children and adults have improved over the years. Part of this progress is due to discovering new genetic mutations that drive these diseases. Imatinib was the first in a series of small-molecule drugs called tyrosine kinase inhibitors (TKIs). It targets a specific abnormal protein called BCR-ABL, which forms because of a chromosomal change known as the Philadelphia chromosome. This protein plays a key role in chronic myelogenous leukemia (CML). While imatinib has been very effective for many patients, about one-third of high-risk CML patients develop resistance to it. Resistance can happen in different ways. It may result from reduced drug uptake into the cancer cells, increased removal of the drug from the cells, overproduction of the BCR-ABL protein, or mutations in BCR-ABL that prevent the drug from working.Resistance can be present from the start (innate) or develop after treatment begins (acquired). Understanding these genetic mechanisms through modern sequencing helps doctors choose the best treatment and improve outcomes for patients(16).

Pharmacogenomics Today

The liver enzyme family called cytochrome P450 (CYP) plays a central role in breaking down more than 30 different types of drugs. People can have genetic differences in the genes that produce these enzymes, which can affect how well their bodies process medications. Some individuals may have versions of CYP enzymes that work poorly or not at all, making it harder for their bodies to remove certain drugs. This can increase the risk of the drugs building up in the body and causing harmful effects or overdoses.Today, researchers use genetic testing to detect variations in CYP genes. This helps them choose the right patients for clinical trials and monitor how they respond to medications. Pharmaceutical companies also test how new drugs are processed by different forms of CYP enzymes to ensure they are safe and effective for people with diverse genetic profiles(17).

The Future of Pharmacogenomics

In the future, pharmacogenomics is expected to reshape drug development in several important ways:

1. Targeted drug design: Creating medicines that interact more precisely with their intended receptors.
2. Optimized absorption and distribution: Ensuring drugs reach the right parts of the body efficiently.
3. Safer drug elimination: Improving how drugs are metabolized and removed from the body to reduce side effects and increase safety.

These advances will make medicines more personalized, allowing treatments to be tailored to each patient's unique genetic makeup for better outcomes and fewer complications.

II. PHARMACOGENOMICS IN CANCER CARE: PERSONALIZED TREATMENT APPROACHES

1. Breast Cancer

For triple-negative breast cancer, chemotherapy remains the main treatment. However, targeted therapies have improved outcomes. For patients with BRCA1/2 mutations, PARP inhibitors such as olaparib and talazoparib, often combined with cisplatin or carboplatin, can enhance treatment effectiveness.

Immune therapies are also showing promise. For instance, atezolizumab, when used with paclitaxel, is effective in patients with PD-L1 positive triple-negative breast cancer. Research on other immune checkpoint inhibitors is ongoing, and more FDA approvals are expected in the near future(18).

2.Antiemetic Therapy

5-HT3 (5-hydroxytryptamine type 3) receptor blockers are the main drugs used to prevent nausea and vomiting caused by chemotherapy or radiation therapy. These medications are broken down in the

liver by enzymes such as CYP2D6, CYP3A4, and CYP1A2 into inactive forms.Some patients are CYP2D6 ultrarapid metabolizers, meaning their bodies process certain drugs, like ondansetron, much faster than usual. This rapid breakdown can make ondansetron less effective at controlling nausea and vomiting in these patients.

To address this, clinical guidelines recommend using an alternative drug that is not primarily metabolized by CYP2D6. For example, granisetron, which is mainly processed by CYP3A4 and CYP1A1, is a better option for patients who are CYP2D6 ultrarapid metabolizers. Other drugs in the same class, such as dolasetron and palonosetron, are also metabolized by CYP2D6. However, there is still limited evidence on how to use CYP2D6 genetic information to guide treatment with these medications(19).

3.Pain Management:
Cancer patients often suffer from two main types of pain:
1.Nociceptive pain – usually treated with opioids.
2.Neuropathic pain – often treated with tricyclic antidepressants (TCAs).
Pharmacogenomics testing can help doctors choose the best medication and dose for each patient.

Some opioids, like codeine and tramadol, need the enzyme CYP2D6 to become active in the body.

- Ultrarapid metabolizers produce too much active drug, which can be dangerous and cause serious side effects.
- Poor metabolizers produce too little, so the drug may not relieve pain.

Guidelines recommend avoiding codeine and tramadol in these patients.
Other opioids, like hydrocodone and oxycodone, are partly active on their own, but their metabolites provide stronger pain relief. The impact of genetic differences on these drugs is less clear, but testing can still help improve pain control for some patients
For neuropathic pain, TCAs like amitriptyline are processed by enzymes CYP2C19 and CYP2D6.

1.At low doses (typical for neuropathic pain), most patients are safe regardless of genetics.
2. Patients who are ultrarapid CYP2D6 metabolizers may not get enough drug, so TCAs should be avoided in them.
3.Other patients can usually take normal doses safely,but caution is needed if multiple genetic variations exist(20).

4.Antidepressant Therapy:
Cancer and its treatment can cause depression. Genetic testing can guide antidepressant selection and dosing.

Genes like CYP2D6 and CYP2C19 affect how certain SSRIs (e.g., paroxetine, fluvoxamine, citalopram, escitalopram, sertraline) are metabolized:
1.Ultra rapid metabolizers may not get enough drug, leading to poor response.
2 Poor metabolizers may have high drug levels and side effects.

Adjusting the drug choice or dose based on genetics can improve treatment. TCAs can also be used for depression, following the same genetic guidance.

5.Antifungal Therapy:
Chemotherapy patients are more prone to fungal infections. Pharmacogenomic testing can help guide antifungal use.Voriconazole is broken down by CYP2C19:

1. Rapid or ultrarapid metabolizers may not reach effective levels; alternative drugs are recommended.
2. Poor metabolizers may have too high levels, increasing the risk of side effects such as liver or neurological problems. Dose adjustments or alternative drugs are advised(21).

6.Tumor Lysis Syndrome Management:
Tumor lysis syndrome occurs in some cancer patients and causes high uric acid levels. Drugs like rasburicase are used to lower uric acid. Rasburicase produces hydrogen peroxide, which can be harmful if the body cannot neutralize it. The enzyme G6PD helps protect cells from this stress.

- G6PD-deficient patients cannot handle oxidative stress and may develop hemolytic anemia.

- The FDA recommends screening at-risk patients (e.g., of African or Mediterranean ancestry) before using rasburicase.

Pharmacogenomics helps identify patients at risk of side effects, allowing doctors to tailor treatment safely and effectively(22).

Personalized Medicine

Personalized medicine is an approach that uses modern molecular and genetic tools to better understand and manage a patient's health or their risk of developing a disease. The main goal is to help doctors and patients make more informed decisions about treatments and care plans that are most likely to work for each individual, taking into account their unique genetic makeup and environmental factors.Genetic differences between individuals can influence how well a person responds to a particular drug. Personalized medicine aims to use this information to develop safer and more effective therapies tailored to specific groups of patients with shared genetic characteristics.

Beyond medications, personalized medicine may also involve lifestyle recommendations, such as diet, exercise, or other interventions, to delay the onset of disease or reduce its impact. By combining genetics, environment, and lifestyle, this approach seeks to provide the most effective and individualized care possible(23)

Market Justification for Pharmacogenomics

The vision of pharmacogenomics revolves around three key objectives:

1. Enhancing drug effectiveness and minimizing risks to patients.
2. Creating diagnostic tools that help guide treatment decisions and improve patient care.
3. Improving outcomes in clinical drug development, making the process more efficient and reliable.

At the same time, these objectives must be achieved in a way that is economically viable. Pharmaceutical companies need to see a clear financial benefit for investing in pharmacogenomics. Since pharmacogenomics often targets smaller patient populations(24) its success depends on balancing the smaller market size with reduced development costs or the ability to charge premium prices for specialized treatments.

Ethical Issues in Pharmacogenomics

A major ethical concern in pharmacogenomics is the privacy of participants(25) People taking part in genetic studies need to clearly understand how their genetic material will be handled. This includes knowing what tests will be performed, how their data will be used, where their DNA will be stored, and how securely it will be protected.Participants should also be informed about who will have access to their genetic information and whether their DNA might be used in future research. Consent for any potential future use of genetic material should be obtained ahead of time.

Family privacy is another important issue. Some genomic studies require information about a participant's relatives, which may not always be acceptable to them. In some cases, experts even suggest that patients might not be given access to their own genetic results to prevent anxiety or worry about possible future health risks(26).

Pharmacogenomics has the potential to improve medical care and increase life expectancy, but it also raises important ethical and societal questions. Advanced genetic-based treatments can be expensive, meaning that only those who can afford them might benefit. From an ethical perspective, access to such care should be equitable, and governments may need to subsidize pharmacogenomic technologies to ensure wider availability.In countries like India, where public health priorities such as access to safe food are urgent, spending large sums on genetic research and tailored therapies may be questioned. In contrast, in countries like the USA, where adverse drug reactions contribute significantly to illness and hospitalizations, pharmacogenomics can help prevent these reactions by guiding drug choices based on an individual's genetic profile(27).

The high cost of genome analysis and concerns about personal autonomy must also be carefully considered. Furthermore, the financial interests of pharmaceutical companies in creating highly specific, low-risk drugs could conflict with ethical research practices and the protection of individuals' rights.It is also important to recognize that genetics is only part of the picture.

Environmental factors, lifestyle, and other variables also influence how a person responds to medication. Relying solely on genetics to guide drug development and treatment may not always be ethically acceptable, and a balanced approach that considers both genetic and non-genetic factors is essential(28).

Legal Issues in Pharmacogenomics

As pharmacogenomics advances, several legal concerns must be addressed before it can be fully implemented.A major question is who owns a person's genetic data once they consent to have it analyzed. What happens if that data is lost, stolen, or accidentally made public? Who is legally responsible, and what compensation is available if harm occurs?Another key concern is consent for future use. If a person's genetic information is used in ways they did not approve, what are the legal consequences? Can individuals refuse to allow their data to be used at any stage of drug development or research? There are also questions about how much information doctors or hospitals need to share. Some experts believe participants should only be informed about the specific condition being studied, rather than being told about potential future risks that may be uncovered from their genetic data.Finally, there is the risk of genetic discrimination. Legal protections are necessary to prevent employers or insurance companies from making decisions based on a person's genetic information (29).

Pharmacogenomic information can have important social and ethical implications. For instance, if employers have access to a person's genetic data, they might hire only those whose genes indicate a better fit for the job. While this may benefit companies, it can discriminate against others, leaving some people unemployed or forcing them to make difficult choices to earn a living. Similarly, insurance companies might deny coverage based on genetic predispositions, creating additional ethical and social concerns.The economic burden of new pharmacogenomic therapies often falls on society as a whole. Moreover, knowing one person's genetic information can inadvertently reveal details about their family and community, potentially breaching privacy since consent from these relatives may not have been obtained. By constructing family trees from genetic data, predictions can be made about disease risks, drug responses, or susceptibility to conditions—even those currently untreatable (30) This knowledge has both advantages and drawbacks. On the positive side, it allows for early lifestyle adjustments, preventive measures, and timely medical interventions, which can improve health outcomes and increase longevity. On the negative side, knowing about a serious, untreatable
genetic risk could cause psychological distress long before the disease develops.

Pharmacogenomic findings may also raise legal or constitutional issues, such as eligibility for special incentives or minority status, adding further complexity to their social and ethical impact(31)

Anticipated Benefits of Pharmacogenomics

1. More Precise and Effective Medicines

Pharmaceutical companies will be able to design drugs based on the specific proteins, enzymes, and RNA molecules associated with genes and diseases. This precision allows for therapies that directly target the disease, maximizing effectiveness while protecting healthy cells(32).

2. Safer Treatments

Rather than relying on the traditional trial-and-error approach, doctors can use a patient's genetic profile to prescribe the most suitable medication from the start. This approach reduces guesswork, speeds up recovery, and lowers the risk of adverse reactions. In the United States alone, pharmacogenomics could prevent thousands of deaths and millions of hospitalizations caused by drug-related complications each year(33).

3. Personalized Dosages

Instead of basing drug doses solely on weight or age, treatment can be tailored to a person's genetic makeup. This ensures that the drug is processed efficiently, maximizing therapeutic benefit while reducing the risk of overdose(34).

4. Early Disease Detection and Prevention

Knowing one's genetic information allows individuals to make early lifestyle changes to prevent or reduce the severity of genetic conditions. It also enables closer monitoring and timely interventions, ensuring treatments are introduced at the most effective stage(35).

5. Improved Vaccines

Vaccines made from DNA or RNA offer all the benefits of traditional vaccines without the risk of causing infection. They are safe, cost-effective, stable, easy to store, and can even be engineered to target multiple strains of a pathogen simultaneously(36).

6. Faster and More Efficient Drug Discovery

Pharmacogenomics helps pharmaceutical companies identify promising therapies more quickly by focusing on specific genetic populations. Drugs that previously failed may find success when matched to the right patient group. Clinical trials become more efficient and cost-effective by including only Patient likely to respond, reducing,both risk and expense (37).

7. Lower Healthcare Costs

By improving the precision and safety of treatments, pharmacogenomics can reduce overall healthcare costs through(38):

- Fewer adverse drug reactions
- Fewer failed drug trials
- Faster drug approval processes
- Shorter treatment durations
- Reduced need for multiple medications
- Early detection and treatment of diseases
- Broader range of effective therapies.

Expectations and Future Possibilities

Reviving Previously Failed Drugs

Around 10% of drugs are withdrawn in the years after FDA approval, often due to toxicity or lack of effectiveness. Pharmacogenomics offers a way to bring some of these drugs back into use(39).Many drugs fail in clinical trials because their effects vary among individuals. The level of toxicity can depend heavily on how a person metabolizes the drug. By tailoring doses to a patient's genetic profile, it becomes possible to reduce side effects and safely use drugs for those most likely to benefit(40).In other words, pharmacogenomics allows us to focus treatments on specific genetic groups, making previously abandoned drugs safer and more effective. This approach balances the general effectiveness of a drug with the individual responses of patients, providing new opportunities for therapies that were once considered unsuitable(39)

Balancing Drug Effectiveness and Safety

For a drug to work well, it must reach a critical level in the body's target tissue for a sufficient amount of time. If the drug level is too low, it won't be effective; if it's too high, it could become toxic.This delicate balance depends on both the dose of the drug and how the body processes it. Since drug metabolism varies between individuals due to genetic differences, such as variations in the cytochrome P450 enzymes, pharmacogenomics can use this information to determine the optimal dose for each person.

Many pharmaceutical companies are already considering these genetic and metabolic differences to improve both the effectiveness and safety of drugs. This strategy is especially useful in cancer therapy, where even small variations in how a patient metabolizes chemotherapy can determine whether the treatment is effective or dangerously toxic(41).

Challenges

Pharmacogenomics is still a developing and emerging field. Since it is in its early stages, there are several challenges and barriers that must be addressed before it can be widely used in healthcare. These include understanding complex genetic interactions, integrating genetic testing into routine medical practice, and overcoming technical, ethical, and regulatory hurdles.

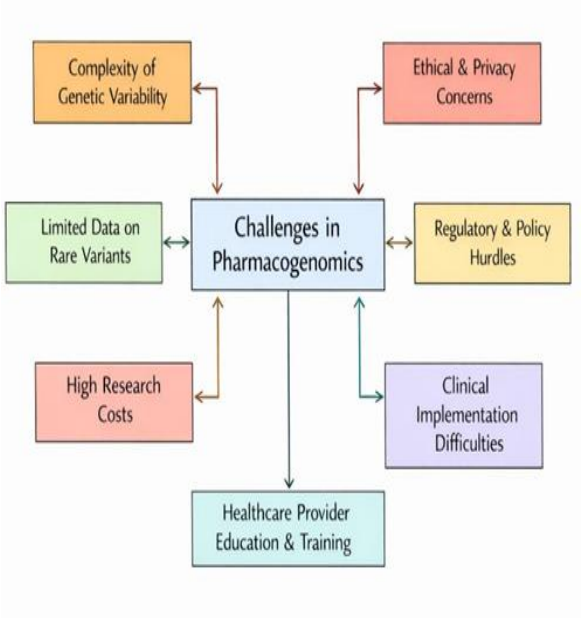

Fig 2: Challenges in Pharmacogenomics

Limitations of Pharmacogenomics

A person's response to a drug is often influenced by many different genes, which makes predicting drug reactions and developing targeted treatments quite complex. Everyone carries small genetic differences that usually do not affect normal gene function. However, some of these variations can impact how a drug is metabolized or how a disease progresses, so they need to be carefully identified and studied(42) This process is challenging and time-consuming. In addition, non-genetic factors such as interactions with other medications, lifestyle, and environmental influences can also affect how a drug works. All of these factors must be considered before drawing accurate conclusions about the Role of genetics in drug response(43).

III. BARRIERS TO PHARMACOGENOMICS

1.Drug Labels

In recent years, more drug labels include information about pharmacogenomics (PGx). This can help predict how a patient might respond to a standard drug dose, including potential side effects. However, the best way to apply this genetic information for prescribing decisions—such as selecting the right drug or adjusting the dose—is still not fully clear.

2.Evidence Limitations

A major barrier is the lack of strong, consistent evidence demonstrating that PGx improves patient outcomes compared to traditional medical practice. Most studies are small, and the relationships between genetic variations (genotype) and drug responses (phenotype) are often complex. This makes it difficult to apply PGx reliably in everyday clinical settings.

3. Clinical Trials

The limited number of controlled clinical trials is another challenge. Only a few randomized trials have tested the clinical usefulness of genotype-based treatment, such as for warfarin (bleeding or clotting risk), abacavir (hypersensitivity reactions), and tacrolimus (target blood levels). Larger trials are needed to fully understand the benefits of PGx-guided therapy.

4 Education and Training

Doctors make the final decisions about prescribing drugs. Studies suggest that better education in pharmacogenomics during undergraduate and postgraduate training would help clinicians use PGx more effectively. Currently, a lack of training and knowledge among healthcare professionals is a significant obstacle. While some programs introduce PGx at the postgraduate level, it would be more effective to start education earlier, at the university or bachelor's degree level.

Application of Pharmacogenomics

Pharmacogenomics plays a key role in understanding and treating diseases with a strong genetic component. Many common conditions, such as obesity and diabetes, have well-established genetic links, and studies like sibling analyses help estimate how much genetics contributes to these diseases.

Even rare genetic mutations can reveal important insights into complex biological processes. For example, a patient with unusually high HDL (good cholesterol) levels can help illustrate how the CETP (cholesterol ester transfer protein) gene affects HDL levels. Similarly, mutations in the JAK3 gene can lead to severe combined immunodeficiency syndrome, providing clues about how JAK3 inhibition might impact immune function.

These findings have guided the development of new drugs targeting CETP and JAK3. Thanks to pharmacogenomics, the connections between genes and disease are becoming clearer, allowing doctors to choose therapies that are better tailored to a patient's genetic makeup.

Uses of Pharmacogenomics

Pharmacogenomics is currently applied on a limited scale but plays an important role in improving drug safety and effectiveness. One key application involves the cytochrome P450 (CYP) family of liver enzymes, which are responsible for breaking down more than thirty classes of medications (44),(45).

Genetic variations in the genes that produce these enzymes can affect how well a person metabolizes certain drugs. Some individuals may have less active or inactive forms of CYP enzymes, which can prevent medications from being properly broken down and eliminated from the body, potentially leading to overdoses or severe side effects.

Today, researchers in clinical trials use genetic testing to detect variations in CYP genes, helping to guide patient selection and monitoring. Pharmaceutical companies also test new drugs to see how efficiently they are metabolized by different CYP enzyme variants(46).

Another important example is thiopurine methyltransferase (TPMT), an enzyme that metabolizes thiopurine drugs used in treating childhood leukemia. A small percentage of people, particularly among Caucasians, have genetic variations that make TPMT inactive. Without active TPMT, thiopurine drugs can accumulate to dangerous levels, increasing the risk of toxicity(47).

IV. CONCLUSION

Pharmacogenomics is a powerful and largely untapped tool in the pharmaceutical industry, offering the potential to maximize the benefits of medicines. It marks a significant leap forward in the history of medicine. Its main objectives include personalized therapy based on an individual's genetic profile, increasing drug effectiveness while reducing side effects, linking genetic variations with clinical outcomes, identifying new drug targets, and using genetic profiling to determine disease risk and predict responses to medications.

Traditionally, most drugs were developed to work for the average person, not for each individual. Pharmacogenomics is changing this approach, allowing treatments to be customized for specific patients, making drugs more effective and safer. Instead of relying only on visible symptoms, doctors can now analyze a patient's genetic makeup and tailor therapy accordingly—this approach is known as phenotypic pharmacogenomic medicine. Gradually integrating pharmacogenomic testing into drug discovery and development is expected to lower development costs while improving patient outcomes.

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