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CONTINUINGMEDICAL EDUCATION

Basic Cytogenetics and Karyotyping: Initial Step for Identification of Genetic Disease

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Abstract
Genetic disorders are conditions that arise from alterations in the DNA sequence, which can be inherited or occur spontaneously. These alterations may affect a single gene or multiple genes, and they can also be influenced by environmental factors. Knowledge about the importance of suitable cytogenetic tests, the challenges faced in cytogenetics, the importance of pre-investigation lab work, and post-lab communication are important for the establishment of any cytogenetic lab. Continuous medical education can help in upgrading the knowledge and skills of Medical Practitioners.

Keywords
Base Sequence; Pregnancy, Multiple; Cytogenetic Analysis; Communication; Education, Medical

Introduction
Throughout history, humanity has grappled with a wide array of diseases. Advancements in therapeutic options have led to a shift in priority areas. While infectious diseases and nutritional deficiencies were once the primary focus, developing vaccines and antibiotics has allowed us to successfully eradicate some infectious diseases and control nutritional deficiency conditions through national nutrition programs and interventions. As a result, attention is now turning towards non-communicable diseases, with India experiencing a notable transition in this direction. Among non-communicable diseases, rare genetic disorders are a significant concern.

Genetic disorders not only affect the physical health of the patient but also have a negative impact on the psychological and financial well-being of the patient and their family. Any data that can contribute to the existing knowledge about genetic anomalies will help in the planning of support and counseling facilities for genetic diseases, ultimately improving the quality of life for the patient and their family. It also assists in the development of policies to prevent conditions or factors that can lead to genetic disorders.

Cytogenetics is a branch of biology focused on the study of chromosomes especially as applied to medical genetics. Cytogenetics may be used to help diagnose a disease or condition, plan treatment or find out how well treatment is working. Karyotyping is one of the

oldest genetic methods available. It describes the number and appearance of chromosomes. Karyotyping is typically performed on dividing cells (like peripheral blood, bone marrow, placenta, and tumor mass) to create a karyogram, which is a visual representation of condensed metaphase chromosomes arranged in matching pairs by size. This allows for the analysis of the microscopic appearance of somatic chromosomes during cell division.

Before the development of staining techniques, it was difficult to detect the structural details of chromosomes using a light microscope. To improve analysis, cytologists have created stains that bind with DNA, producing distinct banding patterns for different chromosomes. This has made it much easier to distinguish between chromosomes, as before these techniques, they were primarily grouped based on size and centromere placement.

The G-banding method is a common staining technique that uses the Giemsa stain to create chromosome-specific patterns known as G-banding. These "bands" are differently stained light and dark areas on the chromosomes. Dark bands are created in AT-rich areas and GC-rich areas appear as light bands. G-banding can help recognize a wide range of structural abnormalities or rearrangements of chromosomes, such as translocations, additions, deletions, and inversions. (1)

Molecular cytogenetics is an evolving field, with ongoing development of new diagnostic methods. As these new technologies are integrated into clinical practice, we anticipate that cytogeneticists will become increasingly efficient in transitioning from analyzing karyotypes to studying genes.

Cytogenetic testing is required for abnormal prenatal biochemical screening tests or ultrasound findings. It is also useful in cases of developmental delays, autism, and intellectual disability. Cytogenetic analysis can be used for cancer diagnosis and selection of appropriate therapy with better prognosis. (2)

Chromosome analysis using NGS yielded similar results to conventional G-banding and was able to detect segmental aneuploidy or mosaicism. NGS-based analysis does not necessitate cell culture or a large number of cells, and it can examine cases that are challenging to analyze using conventional G-banding. (3)

At present several new medical institutes are opened in India and they are in the process of establishing various labs and other facilities for providing better health care. Cytogenetics is an area that is yet to be explored by most institutes. The establishment of a Cytogenetic lab can help in getting diagnostic information for birth defects, bad obstetric history genetic disorders, and cancers timely and at their setup.

The training sessions for fundamental culture techniques in cytogenetics can cover various aspects. This includes preparing culture media, taking necessary precautions, and learning protocols for different culture samples. It should involve the preparation of stains and chemicals essential for karyotyping, as well as the karyotyping process, slide preparation, staining techniques, and elucidating banding patterns on the chromosomes. Additionally, it covers the different types and groups of chromosomes based on centromere location and the various bands that appear after Giemsa staining. Furthermore, it includes studying various structural chromosomal abnormalities, elaborating on their visual manifestations, and their nomenclature, usage of software to modify chromosomes, troubleshooting, and reporting of the ideograms.

Strength of G banding technique of Karyotyping:

- It can be done on cells like Peripheral blood, bone marrow, chorionic villi, amniotic tissue, solid tissue, tumors, etc.
- Require equipment and instruments commonly available in a secondary or tertiary health care setup.
- It is a sensitive diagnostic test
- It is useful for both screening and diagnosis of the genetic disorder

Weakness of G banding technique of Karyotyping:

- Require fresh samples
- Expertise in each step of karyotyping is required for appropriate result

- Time-consuming (culture of sample requires 72-96 hours)
- After initial diagnosis for more specific diagnosis like in cases of cancers other techniques like FISH or molecular cytogenetic techniques are required (4)

Multiple myeloma (MM), the second most common hematological malignancy is a type of cancer. The current understanding of MM's development involves chromosome translocations or alterations in chromosome number, which can result in hyperploidy. Around 40% of patients with MM have primary translocations, often linked to a hypodiploid karyotype. The use of banding analysis and FISH for high-risk aberrations helps to understand the complexity of high-risk Multiple Myeloma better. (5)

A study compared the results of conventional karyotyping and FISH analysis in hematological malignancies such as multiple myeloma cases. The study observed that FISH alone may not detect cytogenetic abnormalities of prognostic significance, such as monosomy 16, loss of Y, or various trisomies. Therefore, conducting both tests together will provide valuable information in the cytogenetic workup of multiple myeloma and may uncover new cytogenetic aberrations with potential prognostic significance. (6)

A study by Tatiana et al found that chances of recurrent pregnancy loss not related to any associated pathology are more common among the older age group. Chromosomal anomalies or aberrations are associated with 46.6% of cases of recurrent pregnancy loss. (7)

The development of each new molecular technique may seem to signal the end of cytogenetics. However, cytogenetics remains the first approach for diagnosing genetic disorders in patients with intellectual disabilities and malformations, making it an indispensable tool. Despite the introduction of new molecular techniques, cytogenetics continues to be widely used for various applications, including clinical diagnostics and basic genomic research. (8)

The landscape of rare diseases in India posed significant challenges due to limited awareness, inadequate testing infrastructure, and minimal attention to diseases that affect a small portion of the population. For a considerable period, both the scientific community and policymakers remained uninformed about rare diseases. Awareness, scientific advancements for understanding these conditions, and the development of treatment options are still in their infancy. Despite the numerous obstacles in this domain, the Ministry of Health and Family Welfare, Government of India, crafted a National Policy for Rare Diseases (NPRD 2021). This policy was designed to implement both short-term and long-term strategies to address rare diseases comprehensively and holistically. (9)

Rare genetic diseases, though individually rare, collectively have a significant impact on morbidity and mortality. There are over 9,000 documented rare diseases, impose a heavy burden on patients, families, and the healthcare system. Diagnosis for rare genetic diseases can be a long and challenging process, with about 50% of patients remaining undiagnosed. A mission program on paediatric rare diseases aims to study unique clinical conditions using advanced technologies, providing diagnoses, and establishing a platform for rare disease research and treatment. (10)

CONCLUSION

Continuous medical education programs (seminars, symposiums, workshops, etc.) can be used as tools for the upgradation of knowledge and skills of doctors. A hands-on workshop-like learning experience for one or two days about culture techniques, slide preparation &staining techniques, and interpretation of Karyotyping results can help in the capacity building of medical practitioners. These training sessions or workshops on the basics of the establishment of a cytogenetics lab and basic cytogenetic techniques of Karyotyping like G banding can encourage doctors to work in this area. It will help them identify and manage cancers and other genetic disorders at an early stage.

Authors Contribution

All authors have contributed equally.

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Conflict of Interest

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Declaration Of Generative AI And AI Assisted Technologies In The Writing Process

The authors haven't used any generative AI/AI assisted technologies in the writing process

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