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## **A review study on genetic disorder diseases**

**Ajaz Ur Rasool**

Research Scholar B.U Ajmer India

**Dr Poornima Shrivastava**

Professor Bhagwant University Ajmer Rajasthan

**Abstract**--Human beings are exceedingly assorted. In general variation is due to genetic differences. Individual differ from one another in their normal physiological and mental attributes. Variations can be normal or abnormal. They also differ in their susceptibilities for particular disease or other abnormalities. These variations are due to genetic as well as environmental factors. There is strong evidence that genetic factors play an important role in human diseases. In the technologically developed countries, genetic disorders and birth defects are emerging as a major health problem, especially after eliminating malnutrition and endemic diseases, and having better control over epidemic and environmental disorders. In this paper we also discuss the different types of the genetic disorder and bring a small conclusion on it.

**Keywords**--genetic disorders, gene inheritance, chromosome abnormalities, mendelian inheritance.

### **Introduction**

be due to a single base change, small insertions or deletions, splice defects or larger copy number variations which could be translocations, duplications or larger deletions (greater than 1MB) It could even be an addition or deletion of an entire chromosome or part of a chromosome. Loss of such genetic material cause specific or complex Genetic disorders are caused by variations in individual's DNA. The abnormalities may phenotypes. The inheritance of traits from one generation to the next follows certain laws proposed by George Mendel, popularly known as Mendelian inheritance. They are the law of independent segregation, Law of independent assortment and the law of dominance. Genomic variations in the protein coding regions may alter the protein functions and have the potential to cause a disorder. It could be a single gene disorder (monogenic disorders), multi genic disorders which are caused by mutations in more than one gene or multifactorial disorders with additional complexities due to environmental factors.

For example, achondroplasia is a monogenic disorder of human short limbed dwarfism that occur as a result of a mutation in the gene that codes for the fibroblast growth factor receptor. Diabetes is a multifactorial disorder where the disease risk is increased by the environmental factors. Several genes that underlie the human genetic disorders have been studied even before the human genome was sequenced using linkage-based methods. The aetiology of genetic disorders were elucidated by carrying out classical genetic analysis such as linkage analysis, candidate gene analysis, cytogenetic studies, fluorescence in situ hybridization (FISH) and array CGH methods. These procedures are laborious, time consuming, costly and have several pitfalls. Linkage methods provide an association but to identify causative genes for complex disorders such as obesity, hypertension, intellectual disability and diabetes which we have to resort to next-generation based sequencing methods. Recently, next-generation sequencing methods and the availability of the draft of the human genome have the incredible potential to identify the causal genomic variations quickly and with high precision. It is becoming the method of choice which could reveal the causal genes for any monogenic and as complex disorders. Mendelian inheritance in man (OMIM) is an online catalogue of phenotypes and causative genes associated with several genetic conditions in humans. The data available in OMIM are manually curates from literature for over forty years. It provides disease description and clinical synopsis for several Mendelian inherited disorders. As of today, OMIM stores information for about 4,393 phenotypes with known molecular evidence. Among them, 4,070 of them are autosomal, 291 are X-linked, 4 of them are Y-linked and 28 of them are caused by mitochondrial genomic disorders. There are 1,665 phenotypes in OMIM for which molecular basis are still unknown. These remarkable achievements were due to the advancements in the techniques and statistical methods for gene mapping and DNA sequencing to identify the genomic variants associated with a disease.

## **Types Of Genetic Disorder**

### ➤ **Single gene inheritance**

Single gene inheritance is also called Mendelian or monogenetic inheritance. Changes or mutations that occur in the DNA sequence of a distinct gene effect this type of inheritance. There are thousands of known single-gene disorders. These disorders are known as monogenetic disorders (disorders of a single gene). Single-gene disorders have diverse patterns of genetic inheritance, including

- autosomal dominant inheritance, in which only single copy of a defective gene (from either parent) is crucial to basis the condition;
- autosomal recessive inheritance, in which two copies of a defective gene (one from each parent) are necessary to effect the condition; and X-linked inheritance, in which the defective gene is present on the female, or X-chromosome. X-linked inheritance may be dominant or recessive. Some examples of single-gene disorders include
- cystic fibrosis, alpha- and beta-thalassemia, sickle cell anaemia, Marfan syndrome, fragile X syndrome, Huntington's disease, and hemochromatosis.

➤ **Multifactorial Genetic inheritance**

Multifactorial inheritance is also called intricate or polygenic inheritance. Multifactorial inheritance disorders are caused by a permutation of environmental factors and mutations in multiple genes. For example, unusual genes that control breast cancer susceptibility have been found on chromosomes 6, 11, 13, 14, 15, 17, and 22. Some common chronic diseases are multifactorial disorders. Multifactorial disorders also known as complex genetic disorders caused by genomic variations in one or more genes. Environmental factors can increase or decrease the risk of such disorders. For example, coronary artery disease, in which several factors such as high blood pressure, obesity, high levels of low-density lipoprotein cholesterol, type II diabetes and gum diseases increases the risk of the disease. Such disorders occur in isolation and may not follow Mendelian inheritance. Affected children were born to the unaffected parents. Although there could be several members of the family affected, the inheritance does not follow the Mendelian inheritance pattern. The disease may occur in one particular trait but it is not sex-limited trait. The less affected gender will be the carriers of the disease. Although coronary artery disorder runs in a family, it occurs in isolation and does not follow Mendelian inheritance pattern. Multifactorial inheritance also is associated with heritable traits such as fingerprint patterns, height, eye color, and skin color.

➤ **Chromosome Abnormalities**

Chromosomes, distinct structures made up of DNA and protein, are located in the nucleus of each cell. Because chromosomes are the carriers of the genetic material, abnormalities in chromosome number or structure can result in disease. Abnormalities in chromosomes typically occur due to a problem with cell division. The abnormality in the copy number or structure of the chromosomes which leads to a net gain or loss of genetic material causes several human genetic disorders. The genetic disorders caused by abnormal number of chromosomes are known as aneuploidy. In case of monosomy, there is a loss of one chromosome (Turners syndrome) whereas an addition of one chromosome causes trisomy (Down syndrome). Tetrasomy is caused by addition of two chromosomes. Most of the aneuploidies occur due to the improper segregation of chromosomes during meiosis. Incorrect copy number of a particular region of a chromosome or a gene could arise from the chromosome structural aberrations.

➤ **Mitochondrial Genetic inheritance**

This type of genetic disorder is caused by mutations in the non-nuclear DNA of mitochondria. Mitochondria are small round or rod-like organelles that are involved in cellular respiration and found in the cytoplasm of plant and animal cells. Each mitochondrion may contain 5 to 10 circular pieces of DNA. Since egg cells, but not sperm cells, keep their mitochondria during fertilization, mitochondrial DNA is always inherited from the female parent. Examples of mitochondrial disease include

- Leber's hereditary optic atrophy (LHON), an eye disease;
- myoclonic epilepsy with ragged red fibers (MERRF); and
- mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes , a rare form of dementia.

## **Review of Literature**

Khan, A et al,(2015) reported that congenital defects are the chief reason of new born. Each year about 3% of 134 million annual birth are affected by major structural and functional defects. Yu-shik, H et al, (2009) reported that controlling the embryonic stem cell microenvironment has been developed for regulating cellular fate. He used micro engineered hydrogel micro well direct to Es cell differentiation and determine the role of WNT signalling pathway. Angus, C et al, (1996) reported that adherence to agreed protocols and standards of care. It may be simple to evaluate some element of clinical genetic. Akhilesh, P (2015) reported that studied was carried out on a family of Asian Indian ethnicity. Clinical work up related that the type of ID (intellectual disability ) seen in the family as non-syndrome and the pedigree consulted with an X linked recessive mode of inheritance. Joti, A et al (2012) reported that Birth defects including metabolic disorder acquired during embryonic development and present at birth. Children born with major defects how survive infancy are effected physically, mentally or socially and can at increased risk for morbidity for various health disorder, which can be life threatening. The World Health Organization (WHO) has categorized several countries of the world into six regions for estimation of global burden of visual impairment. WHO estimates that 80% of visual impairment is either preventable or curable with treatment. This includes cataracts, blindness due to infections and trachoma, glaucoma, diabetic retinopathy, uncorrected refractive errors, and some cases of childhood blindness. Many people with significant visual impairment benefit from vision rehabilitation, changes in their environment, and assistive devices (Visual impairment and blindness fact sheet, 2014).

## **Medical Knowledge and Solution of Genetic Disorder**

The expansion of knowledge related to genetics is changing our understanding of pathophysiology and influencing our classification of diseases. Awareness of genetic etiology can have an impact on clinical management, including prevention and screening for or treatment of a range of diseases. Primary care physicians are relied upon to help patients navigate testing and treatment options. Consequently, they must understand the genetic basis for a large number of genetically influenced diseases, incorporate personal and family history to determine the risk for a specific mutation, and be positioned to provide counselling. Even if patients are seen by genetic specialists who assess genetic risk and coordinate testing, primary care providers should provide information to their patients regarding the indications, limitations, risks, and benefits of genetic counselling and testing. They must also be prepared to offer risk-based management following genetic risk assessment. Given the pace of genetics, this is an increasingly difficult task. The field of clinical genetics is rapidly moving from single gene testing to multigene panel testing, with techniques such as whole-exome and -genome sequencing on the horizon, increasing the complexity of test selection and interpretation, as well as patient education and medical decision making. Current research into pathophysiological mechanisms has not only shed light on normal and abnormal physiology, but also helped to elucidate underlying pathology behind common disorders. Besides that, the development of more efficacious diagnostic tools have broadened clinical perspectives and led to diverse

applications in the treatment of other diseases too. These would not have been possible if not for the immense collaborative partnerships formed between academia, pharmaceutical establishments, patient-driven organizations and regulatory authorities, underscoring the importance of cooperation. Undoubtedly, delving deeper into rare genetic diseases can provide valuable insights into our current understanding of medicine.

## Conclusion

Single gene inheritance is also called Mendelian or monogenetic inheritance. Changes or mutations that occur in the DNA sequence of a single gene cause this type of inheritance. There are thousands of known single-gene disorders. These disorders are known as monogenetic disorders (disorders of a single gene). Single-gene disorders have different patterns of genetic inheritance, including. Autosomal dominant inheritance, in which only one copy of a defective gene (from either parent) is necessary to cause the condition. Autosomal recessive inheritance, in which two copies of a defective gene (one from each parent) are necessary to cause the condition; and X-linked inheritance, in which the defective gene is present on the female, or X-chromosome. X-linked inheritance may be dominant or recessive. Multifactorial inheritance is also called complex or polygenic inheritance. Multifactorial inheritance disorders are caused by a combination of environmental factors and mutations in multiple genes. For example, different genes that influence breast cancer susceptibility have been found on chromosomes 6, 11, 13, 14, 15, 17, and 22. Some common chronic diseases are multifactorial disorders. Such disorders occur in isolation and may not follow Mendelian inheritance. Affected children were born to the unaffected parents. Although there could be several members of the family affected, the inheritance does not follow the Mendelian inheritance pattern. The disease may occur in one particular trait but it is not sex-limited trait. The less affected gender will be the carriers of the disease. Although coronary artery disorder runs in a family, it occurs in isolation and does not follow Mendelian inheritance pattern. Multifactorial inheritance also is associated with heritable traits such as fingerprint patterns, height, eye colour, and skin colour.

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