Genetic Diseases (Literature Review)

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ABSTRACT

Background. Increased knowledge of genomics over the past two decades has made it increasingly clear that traditional categories of genetic diseases define only those conditions in which the genetic component is most prominent, whereas in fact diseases can be grouped according to a variety of traits representing different combinations of genes and environmental factors. Knowledge of genomics that can benefit humans is only just emerging, and it is anticipated that genomics will "make a significant contribution to public health" in the future.[1]

Chromosomal abnormalities are disruptions in the normal chromosome makeup of a cell and are the leading cause of genetic disease in humans; some chromosomal abnormalities, such as translocations or chromosomal inversions, do not cause disease in carriers, although they may result in a higher proportion of chromosomal abnormalities in the offspring.[3] An abnormal number of chromosomes or sets of chromosomes, called aneuploidy, can cause a lethal condition or genetic disorder. In addition, gain or loss of chromosomal material may result in a genetic disorder (deletion, extra copy such as trisomy). Chromosomal mutations cause changes in entire chromosomes (more than one gene) or the number of chromosomes present[6].

Keywords: Chromosomal abnormalities, diagnosis, prenatal diagnosis.

The risk of chromosomal abnormalities increases with increasing maternal age mainly because non-functional events in meiosis are more likely and lead to trisomies. To make it more complex, we need to add "mosaicism". A "mosaic" is an individual with a combination of two-cell lines with different karyotypes (normal and abnormal). Karyotyping analyzes multiple cells to rule out this possibility[5]. A mosaic condition is not as severe as a completely abnormal karyotype and the features may not be as pronounced and a live birth is possible. Sometimes the mosaic is limited to the placenta ("limited placental mosaicism"). A placenta with an abnormal karyotype (limited placental mosaicism) can result in stillbirth even if the fetus has a normal karyotype; conversely, a placenta with a normal karyotype may result in longer survival of a fetus with a chromosomal abnormality. Rarely, the movement of part of one chromosome to another in a parent is passed on to the child as a partial trisomy (e.g., 6p+ or 16p+), which may not be as severe as a complete trisomy.

- Trisomy 21 (extra chromosome 21): Down syndrome; incidence depends on maternal age, although the type of translocation is familial; features may include: epicanthal folds, simian folds, brachycephaly, heart defects.[7]
- Trisomy 18 (47,XY,+18): features include micrognathia, overlapping toes, horseshoe kidney, rocker feet, heart defects, diapragmatic hernia, omphalocele.[2]

• Trisomy 13 (Patau syndrome, also called D syndrome): features include microcephaly, cleft lip and/or palate, polydactyly, heart defects, holoprosencephaly.
• Trisomy 16: seen in first trimester abortions. Never born alive. • Monosomy X: Turner syndrome (45, X 0); may survive to adulthood; features include short stature, cystic hygroma of the neck (leading to webbing), infertility, coarctation.
• Klinefelter syndrome (XXY, male with 2 X chromosomes); features include long lower body, gynecomastia, testicular atrophy (incidence: 1/500 males)
• Triploidy: there is often a partial hydatidiform mole of the placenta. Fetal features include 3-4 syndactyly, notched nasal bridge, small size.
• Idic 15 or isodicentric 15: inverted duplication of chromosome 15 or tetrasomy 15
• Jacobsen syndrome is also called terminal disorder 11q deletion. It is a very rare disorder. Affected individuals have normal intelligence or mild intellectual disability with poor language skills. Most have a bleeding disorder.
• XYY syndrome. XYY boys are typically taller than their siblings. Like XXY boys and XXX girls, they are slightly more likely to have learning disabilities.
• Triple XXX syndrome. XXX girls are typically tall and thin. They are more likely to have dyslexia.

Genetic disorders are typically classified as single-gene disorders (hemoglobin apathy, cystic fibrosis, and hemophilia) and chromosomal disorders (Down syndrome, among others). These conditions are considered genetic disorders because defects in one or more chromosomes or genes result in abnormal conditions.[9] Multifactorial disorders, on the other hand, where environmental and genetic factors interact, have traditionally not been considered genetic disorders. Multifactorial disorders are usually categorized as either birth defects, such as neural tube defects, cleft lip and palate, or diseases with a genetic predisposition, such as some chronic noncommunicable diseases. In the literature, birth defects are often grouped with genetic diseases because they become apparent during pregnancy, birth, or early childhood. Inpatient genetic services provide care for people with these or other disorders, and birth defects registries contain information on genetic diseases and birth defects. Given this historical association, this report considers both genetic disorders and birth defects. 3. Some genetic disorders, such as haemophilia, are transmitted by the X chromosome (X-linked disorders are more common in males).[13] Other disorders can arise from abnormal genes on any autosomal chromosome: if the gene is dominant, this always leads to a dominant condition, whereas if it is recessive, many disorders only arise when the same gene is inherited from both parents (and are therefore termed recessive).[10] In recessive conditions, a person who carries an abnormal gene on only one chromosome of a chromosome pair may not be affected or may even appear to be in an advantageous condition; for example, people with sickle cell anemia and thalassaemia genes may be protected from malaria. This example shows that environmental factors can confer an advantage on the carriers of a gene and make the gene more common, although it causes disease when inherited from both parents. 4. Genetic diseases can range in severity from fatal before birth to requiring chronic treatment; their manifestations span all stages of life from infancy to old age. When manifested at birth, they are particularly severe, as they can lead to early death or to chronic disease throughout life. Worldwide, at least 7.6 million children are born each year with serious genetic or congenital defects; 90% of these children are born in middle- and low-income countries. Accurate prevalence data are difficult to collect, particularly in developing countries, because of the great variety of conditions and because many cases remain undiagnosed. In the developing world, genetic and congenital disorders are the second leading cause of death in infancy and childhood, with an incidence of 25 to 60 per 1,000 at birth, with the higher rates being based on more complete data. 5. All people are susceptible to disease due to genetic mutations. However, certain social and cultural factors may increase the prevalence of genetic disorders in certain communities. Such factors include the tradition of consanguineous or

consanguineous marriages, which result in higher rates of autosomal recessive conditions, including birth defects, stillbirths, and mental retardation. In addition, maternal age over 35 years increases the risk of chromosomal abnormalities in the newborn. Molecular Analysis The technologies developed for the Human Genome Project, the recent surge in available DNA sequences resulting from it, and the increasing pace of gene discovery and characterization have all facilitated the creation of new technical platforms that have expanded the range of diseases that can be diagnosed prenatally. However, the importance of identifying the disease-causing mutation or the informativeness of associated genetic markers prior to DNA-based prenatal diagnosis continues to be emphasized. Various fluorescence in situ hybridization (FISH) technologies provide increased resolution for the detection of structural chromosome abnormalities that cannot be resolved by more traditional cytogenetic assays, including microdeletion syndromes, occult or subtle duplications and translocations, complex rearrangements involving multiple chromosomes, and marker chromosomes. Interphase FISH and quantitative fluorescence polymerase chain reaction are effective tools for rapid prenatal diagnosis of selected aneuploidies, with the latter considered the most cost-effective if the analysis is performed on a large scale. There is some debate as to whether this approach should be used as an adjunct to karyotyping or whether it should be used as a stand-alone test in selected groups of women. Interphase and metaphase FISH, both as single-probe and multiple-chromosomal probe assays, can provide reliable results in a variety of clinical situations. It should be noted that probe signals may vary both between slides (depending on age, quality, etc. of metaphase spread) and within a slide. When a deletion or rearrangement is suspected, a signal on a normal chromosome is the best control for hybridization efficiency, and the control probe also provides an internal control for the efficiency of the FISH procedure. Depending on the sensitivity and specificity of the probe and the number of cells evaluated, the possibility of mosaicism should be considered and comments made if necessary. Using locus-specific probes, at least 5 cells should be assessed to confirm or exclude an abnormality. Multiprobe analysis: three cells per probe should be assessed to confirm a normal signal pattern. Confirmation is recommended if an abnormal pattern is detected. In prenatal interphase screening, aneuploidy signals should be counteracted in at least 30 cells for each probe set. At least 100 wells should be scored. If hybridization is not optimal, the test should be repeated. If a deletion or other rearrangement is suspected, the results should be confirmed with at least one other probe. Results should preferably be supported by karyotype analysis. This is important when there is a discrepancy between expected laboratory data and clinical referral.[14] Before implementing interphase FISH as a diagnostic method, personnel should be trained in the type of samples to be analyzed. Laboratories should establish standards for classifying observations and interpreting results. More recently, a new method for rapid identification of chromosomal abnormalities has been developed called high-resolution comparative genomic hybridization (aCGH), which provides genome-wide analysis of chromosome copy number and structural changes. Array technology enables the study of genetic causes associated with dysmorphic features, mental retardation, developmental delay, multiple congenital anomalies. The commercial array includes more than 40 abnormalities, including areas of duplication and microdeletions. Evaluation of this method is expected to provide scientifically sound evidence for the stated advantages.

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