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Review

Causes of Chromosome Breakage and Mis-segregation Affecting Pregnancy and Newborn Health: An Insight into Developing Reproductive Health Preventive Strategies

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Abstract

Chromosome abnormalities are a leading cause of pregnancy loss, developmental delays, and birth defects. These abnormalities arise from errors in chromosome structure (breakage) or number (missegregation) during cell division. Understanding the causes of these errors is crucial for developing effective preventive strategies to improve reproductive health. This paper aims to review the known causes of chromosome breakage and mis-segregation, emphasizing their impact on pregnancy and newborn health. It further explores potential preventive strategies for mitigating these risks. A comprehensive literature review

was conducted using relevant databases, focusing on studies investigating the causes of chromosome abnormalities, their impact on pregnancy and newborn health, and potential preventive measures. Several factors contribute to chromosome breakage and mis-segregation, including Genetic Predisposition, Environmental Factors (environmental toxins, radiation), Maternal age, Lifestyle Factors (Smoking, alcohol consumption, and obesity), and Cellular Mechanisms. These abnormalities can manifest as various pregnancy complications, including Miscarriage, stillbirth, birth defects, and developmental Delays. The causes of chromosome breakage and mis-segregation are complex and multifactorial. Understanding these factors is crucial for developing effective preventive strategies. These strategies may include genetic counseling, pre-conception health optimization, environmental hazard mitigation, and advancements in assisted reproductive technologies. Further research is needed to identify specific interventions and personalize strategies based on individual risk factors. Addressing these causes and implementing preventive measures can significantly improve reproductive health outcomes and reduce the incidence of chromosome abnormalities affecting pregnancy and newborn health.

Keywords
Chromosome; abnormalities; strategies; genetic modification; nutrition

1. Introduction

Reproductive health is a crucial aspect of overall health and well-being, and it plays a vital role in developing a healthy society [1]. One of the significant concerns in reproductive health is the high prevalence of chromosomal abnormalities in pregnancies. These abnormalities can result in serious health problems for both the mother and the child, and they can have significant financial, emotional, and social implications for families [2]. To address this issue, it is crucial to have a comprehensive reproductive health strategy in place that focuses on reducing and preventing these abnormalities. Firstly, it is important to understand the root causes of chromosomal abnormalities in pregnancy. These can be genetic, environmental, or a combination of both. Genetic factors such as inherited gene mutations or chromosomal rearrangements can increase the risk of chromosomal abnormalities [3]. Meanwhile, environmental factors such as exposure to toxins, radiation, or certain infections during pregnancy can also lead to these abnormalities [4]. Therefore, any effective reproductive health strategy must address genetic and environmental factors.

Promoting pre-conception care is a crucial aspect of developing a reproductive health strategy for reducing and preventing chromosomal abnormalities [5]. This involves educating individuals about the importance of genetic testing and counseling before conception. By identifying potential genetic risks, couples can make informed decisions about their reproductive options and take necessary precautions to reduce the chances of chromosomal abnormalities in their offspring [6]. ART is a medical procedure that assists with conception and pregnancy. They are used when a couple has difficulty conceiving naturally [6]. Therefore, any reproductive health strategy must also include guidelines and regulations for the use of ART with proper counseling genetic testing

such as genetic compatibility test (GCT) to screen for chromosomal abnormalities in parents and pre-implantation genetics diagnosis (PGT-A; PGT-B) to select euploid embryos in high-risk parents. Notably, PGT is a procedure to identify genetic abnormalities in embryos created through in vitro fertilization (IVF). PGT is typically performed on embryos that are 5-8 days old. A few cells are removed from each embryo and tested for genetic abnormalities. The embryos that are found to be free of genetic abnormalities are then transferred to the woman's uterus. PGT can be a helpful tool for couples who are at risk of having a child with a genetic disorder. PGT can also select embryos for specific traits like sex or eye color. PGT-A (pre-implantation genetic testing for aneuploidy) tests for chromosomal abnormalities. Chromosomal abnormalities can cause a variety of health problems, including mental retardation, birth defects, and miscarriage. PGT-B (pre-implantation genetic testing for monogenic disorders) tests for single-gene disorders. Mutations in a single gene cause single-gene disorders. Single-gene disorders can cause a variety of health problems, including cystic fibrosis, sickle cell anemia, and Huntington's disease. Morphological ultrasound scans can highlight morphological defects associated with chromosomal abnormalities.

Another crucial aspect of reducing and preventing chromosomal abnormalities is promoting healthy lifestyle choices for women during pregnancy [7]. This includes avoiding exposure to harmful substances, maintaining a healthy diet and weight, and avoiding risky behaviors such as smoking and excessive alcohol consumption [7]. These lifestyle factors significantly reduce the risk of chromosomal abnormalities and promote overall reproductive health.

Furthermore, comprehensive prenatal care is essential in detecting and managing potential chromosomal abnormalities in pregnancy [8]. Regular screenings and diagnostic tests can help identify abnormalities early on, allowing for better management and treatment options [9]. Prenatal care also includes providing support and resources for expectant mothers, such as genetic counseling and mental health support, to ensure the best possible outcomes for both the mother and the child [10].

Overall, developing a reproductive health strategy for reducing and preventing chromosomal abnormalities in pregnancy requires a multi-faceted approach. This includes promoting pre-conception care, regulating the use of ART, promoting healthy lifestyle choices, and providing comprehensive prenatal care. By addressing genetic and environmental factors and promoting overall reproductive health, we can work towards reducing the occurrence of chromosomal abnormalities and ensuring the well-being of mothers and their children.

2. Chromosomal Abnormalities

During pregnancy, chromosomal abnormalities can occur in the developing fetus [11]. These abnormalities can have significant impacts on the health and development of the baby, and it is essential for expecting parents to understand the different types of chromosomal abnormalities that can occur during pregnancy [1, 11].

Chromosomal abnormalities refer to changes in a cell's number or structure of chromosomes. Chromosomes are our cells' structures containing our genetic material, or DNA [12, 13]. In a typical pregnancy, each cell in the developing baby should have 23 pairs of chromosomes, for 46 chromosomes [14, 15]. However, sometimes errors can occur during the formation of the sperm or egg, resulting in an abnormal number of chromosomes in the fertilized egg.

One type of chromosomal abnormality that can occur during pregnancy is called aneuploidy [16]. Chromosomes duplicate, couple up, and then split apart during a typical cell division event, ensuring that every newly formed cell has an equal number of chromosomes. However, occasionally, the pairings split apart, resulting in an end cell product with an excessive or insufficient number of distinct chromosomes—a situation known as aneuploidy (Figure 1) [16]. Down syndrome is the most well-known example of aneuploidy, where the baby has an extra copy of chromosome 21 [17, 18].

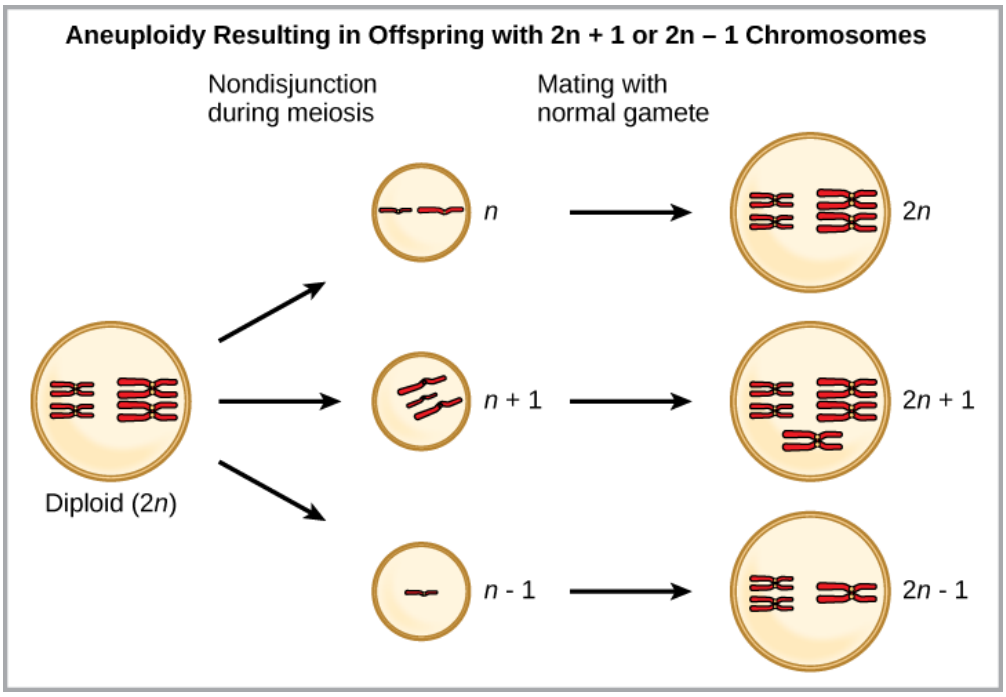

Figure 1 Aneuploidy formation due to non-disjunction during meiosis. When non-disjunction during meiosis causes the gametes to have an excess or shortage of chromosomes, the consequence is aneuploidy. The progeny in this scenario will possess either 2n + 1 or 2n - 1 chromosomes [19].

A cell or organism with an extra set—or sets—of chromosomes is said to be polyploid. Scientists have found two primary forms of polyploidy that can cause a person to become reproductively isolated. The incapacity to interbreed is known as reproductive isolation. We refer to the situation when a polyploid organism possesses two or more complete sets of chromosomes from its species as autopolyploidy (Figure 2). Since the "auto-" prefix means "self," it refers to several chromosomes from the same species. When a meiotic mistake occurs, all chromosomes merge into one cell rather than splitting apart, leading to polyploidy. This situation in humans has nothing to do with reproductive issues except in human spermatids. Polyploidy in human spermatids is a rare condition in which the spermatids contain more than the average number of chromosomes [19]. This can occur due to errors during meiosis, the cell division process that produces gametes (eggs and sperm). Polyploidy can lead to abnormal sperm development and infertility. In humans, polyploidy is most commonly seen in the form of triploidy (three sets of chromosomes) or tetraploidy (four sets of chromosomes) [19]. Triploid spermatids are usually inviable and do not result in fertilization. Tetraploid spermatids, on the other hand, can sometimes fertilize an egg, but the resulting embryo is typically abnormal and does not survive [19].

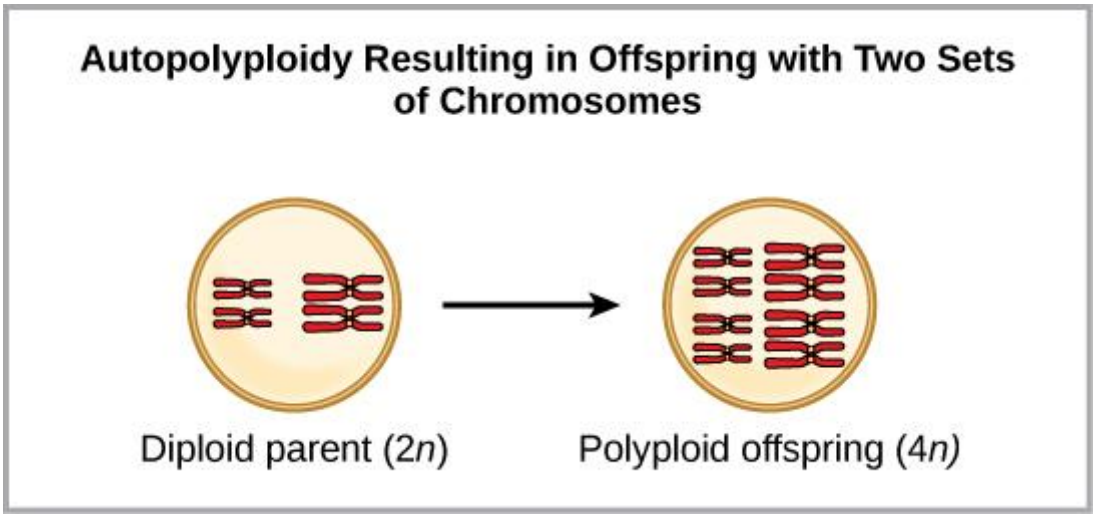

Figure 2 Autopolyploidy formation: When mitosis is not followed by cytokinesis, autopolyploidy occurs [19].

Other examples include trisomy 13, trisomy 18, and Turner syndrome, where the baby is missing one of the sex chromosomes [18]. Another type of chromosomal abnormality is called structural abnormalities [20]. This refers to changes in the structure of a chromosome, such as deletions, insertion, inversion, duplications, or translocations [20, 21]. These anomalies can result in a wide range of phenotypic effects, depending on the affected genes.

a. Deletions: A chromosome is lost when a fragment is deleted. Every portion of a chromosome can have modest or significant deletions (Figure 3a). Any chromosome, at any location and with varying sizes, might experience a deletion. For example, when part of a short arm in chromosome 5 is deleted, this causes Cri-du-chat syndrome, common symptoms of reduced head size and high-pitched crying in infants (Table 1 & Table 2) [20]. A person may experience learning disabilities, delayed growth, and serious health issues if the missing material (the genes) contains vital instructions for the body [21].

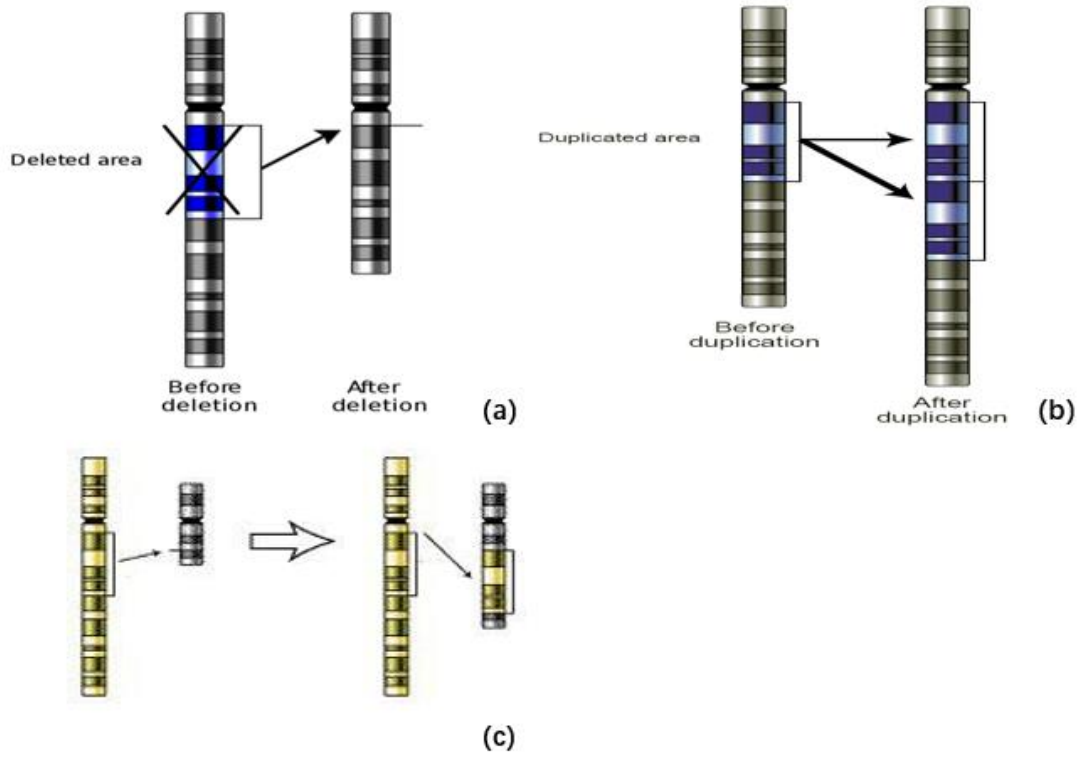

Figure 3 Categories of structural chromosomal anomalies showing (a) Chromosome deletion, (b) Chromosome duplication, (c) Chromosome insertion.

Table 1 Common syndromes associated with structural chromosomal anomalies.

Reference	Structural Chromosomal Anomalies	Common Syndromes
[20]	Deletion	I. Cri du chat syndrome II. Wolf-Hirschhorn syndrome III. Angelman syndrome Prader-Willi syndrome
[20]	Duplication	I. Williams syndrome II. Angelman syndrome
[22]	Inversion	I. Pericentric inversion of chromosome 9 II. Paracentric inversion of chromosome 16
[20, 23]	Translocation	I. Down syndrome (trisomy 21) II. Patau syndrome (trisomy 13) III. Edwards syndrome (trisomy 18)

Table 2 Shows the genetic causes and symptoms associated with various structural chromosomal syndromes.

syndromes	Causes	Symptoms
Cri du Chat Syndrome	Deletion of a small region on the short arm of	High-pitched cat-like cry (hence the name 'cri du chat'), Intellectual disability, Delayed growth and

	chromosome 5 (5p15.2)	development, Facial features: broad face, widely spaced eyes, microcephaly and Heart and kidney defects [23, 24]
Wolf-Hirschhorn Syndrome	Deletion of a large region on the short arm of chromosome 4 (4p16.3)	Severe intellectual disability, Delayed growth and development, Facial features: broad forehead, prominent eyebrows, wide-set eyes, short nose, Heart and kidney defects, and Seizures [25]
Angelman Syndrome (Deletion of Chromosome 15	Deletion of a region on the long arm of chromosome 15 (15q11-q13)	Intellectual disability, Delayed development, Happy and excitable demeanor, Frequent laughter, Balance and coordination problems, Speech difficulties, and Seizures [25]
Angelman Syndrome (Duplication of Chromosome 15q11-q13)	Duplication of a section of chromosome 15, known as 15q11-q13	Severe intellectual disability, Delayed development, Speech impairment or absence of speech, Movement disorders, such as ataxia and tremors, Seizures, Sleep disturbances and Happy and excitable demeanor
Pericentric Inversion of Chromosome 9	Errors in chromosome pairing and recombination can lead to the formation of inverted chromosomes	Growth retardation: Slowed growth and delayed development; Intellectual disability: Cognitive impairment ranging from mild to severe; Craniofacial abnormalities: Unusual facial features, such as a broad forehead and widely spaced eyes; Skeletal abnormalities: Limb and joint deformities, Cardiac defects: Congenital heart malformations; Genitourinary abnormalities: Kidney and reproductive system malformations; and Neurological issues [23]
Paracentric inversion	Similar to pericentric inversions, paracentric inversions can arise during meiosis due to errors in chromosome pairing and recombination	Growth retardation: Slowed growth and delayed development; Intellectual disability: Cognitive impairment ranging from mild to severe; Developmental delays: Speech and language delays, motor coordination difficulties; Craniofacial abnormalities: Unusual facial features, such as a prominent forehead and low-set ears; Skeletal abnormalities: Limb and joint deformities; Neurological issues: Seizures, developmental delays, and behavioral problems; Genitourinary abnormalities: Kidney and reproductive system malformations [23]
Down syndrome	Down syndrome is caused by the presence of an extra copy of chromosome 21, resulting in three copies instead of the normal two. This can occur due to a random error during cell division (non-disjunction)	Distinctive facial features (flattened face, upslanting eyes, small ears); Intellectual disability; Developmental delays; Short stature; Heart defects; Gastrointestinal problems; Skeletal abnormalities; and Increased risk of leukemia and other health issues [20, 23, 25]

	or, more rarely, due to translocation or mosaicism.	
Patau Syndrome (Trisomy 13)	Patau syndrome is caused by the presence of an extra copy of chromosome 13	Severe intellectual disability; Multiple congenital anomalies, including Holoprosencephaly (single fused eye); Cleft lip and palate; Heart defects; Kidney abnormalities; Brain malformations; Short lifespan (most infants die within the first year of life) [23]
Edwards Syndrome (Trisomy 18)	Edwards syndrome is caused by the presence of an extra copy of chromosome 18	Severe intellectual disability; Multiple congenital anomalies, including Microcephaly (small head); Clenched hands with overlapping fingers; Rocker-bottom feet; Heart defects; Kidney abnormalities; Short lifespan (most infants die before birth or within the first few years of life) [20, 23]

b. Duplications: A chromosomal fragment gained is called duplication. In duplication, part of the chromosome is duplicated, resulting in extra genetic material. This occurs in Charcot-Marie-Tooth disease type I, which duplicates part of chromosome 17, causing muscle weakness (Table 1 & Table 2) [20]. Additionally, duplications can affect any portion of a chromosome and can be tiny or enormous. Chromosome duplication occurs when a portion of a chromosome is duplicated or has two copies (Figure 3b). More chromosomal material is the outcome [20, 21]. This excess chromosomal material may induce gene malfunctions that result in health issues, developmental delays, and learning difficulties.

c. Insertions: A segment of a chromosome that has been inserted at an odd location inside the same or another chromosome is known as this sort of chromosomal abnormality (Figure 3c). The individual will be healthy if there is no change in chromosomal makeup. Nonetheless, if chromosomal material is gained or deleted, the individual may experience health issues.

d. Inversion: An inversion is a reversal of the orientation of a segment of a chromosome. Inversions can be pericentric or paracentric (Figure 4). Pericentric inversions are structural chromosomal abnormalities resulting from two breaks, one on either side of the centromere, within the same chromosome, followed by a 180° rotation and reunion of the inverted segment [20, 21]. They can perturb spermatogenesis and lead to the production of unbalanced gametes if (i) the inverted chromosome pairs with a normal one (a homozygote for an inversion has no problems in this perspective) and (ii) if a crossing over occurs within the inverted region (if crossing over is outside this region, it causes no problem). Paracentric Inversions are similar in that they result from two breaks in a chromosome but do not involve the centromere [20, 21]. An inverted region may perform quite typically if it is a balanced inversion or not if it is unbalanced. There may also be other complications as well. The problems that may arise in inversions often manifest during embryonic development in birth defects caused by improper stem-cell differentiation. Problems also occur in somatic cells, leading to diseases such as cancer. Naturally, chromosomal function is frequently very normal if an inversion is balanced because, despite being inverted, a region still has all of its constituent parts in the correct order.

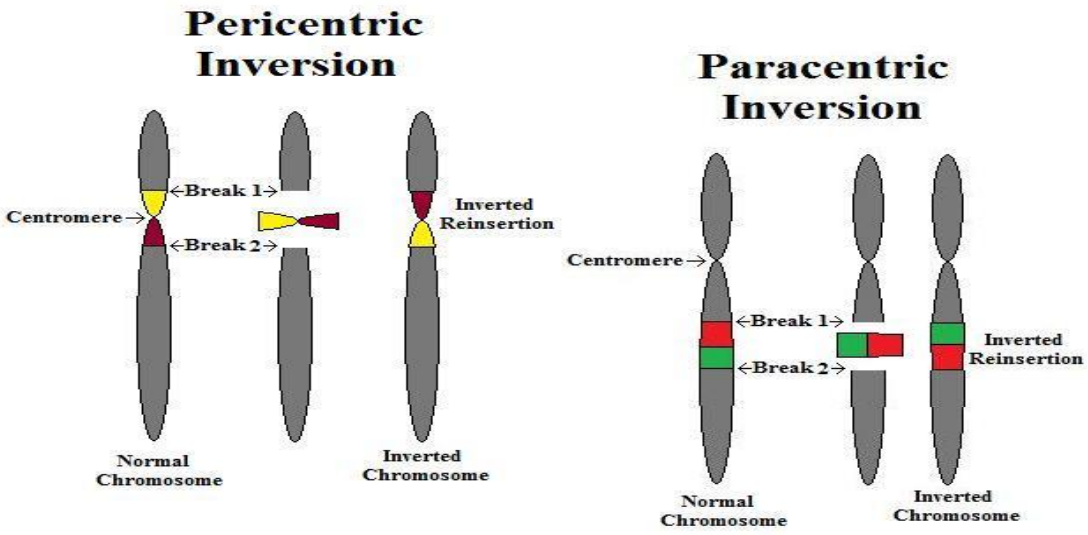

Figure 4 Structure of the pericentric (left) and paracentric (right) inversions (http://newcreationist.blogspot.com/).

e. Translocation: A translocation is rearranging chromosomal material between two or more chromosomes. Translocations can be balanced (involving no loss or gain of genetic material) or unbalanced (involving a loss or gain of genetic material) [20]. It is characterized as an anomaly in the genome where a chromosome breaks and attaches to a separate chromosome whole or in part (Figure 5a). Genetic material can be lost due to chromosomal breakage (deletion) [20, 21]. Additionally, genomic material can be moved and joined to an alternative chromosome, creating a translocation of a chromosome. More so, translocations can cause gene misregulation or develop fusion genes depending on where the breaks occur in a gene or its regulatory regions (Figure 5b). The analysis of various studies has shown a clear correlation between chromosome translocations and infertility. Research has found that chromosome translocations are one of the leading causes of infertility in both men and women [20, 21].

In vitro fertilization (IVF) involves a multi-step process that begins with stimulating the ovaries to produce multiple eggs. These eggs are retrieved and fertilized with sperm in a laboratory setting. The fertilized eggs, called embryos, are cultured for several days before being transferred back into the woman's uterus. The process is meticulously monitored to ensure the highest chances of successful implantation and pregnancy. Studies have shown that individuals with chromosome translocations have a higher risk of experiencing recurrent miscarriages, failed IVF cycles, and other fertility issues [22]. In men, this can lead to reductions in testicular volume and testosterone level, which may impact spermatogenesis, resulting in azoospermia or oligozoospermia and male infertility [21]. At the same time, in women, it can cause recurrent miscarriage and embryo implantation failure [22]. Furthermore, the severity of the impact of chromosome translocations on fertility can vary depending on the specific type of translocation and its location on the chromosome. Individuals with balanced translocations, where no genetic material is lost, may have a better chance of conceiving naturally than those with unbalanced translocations.

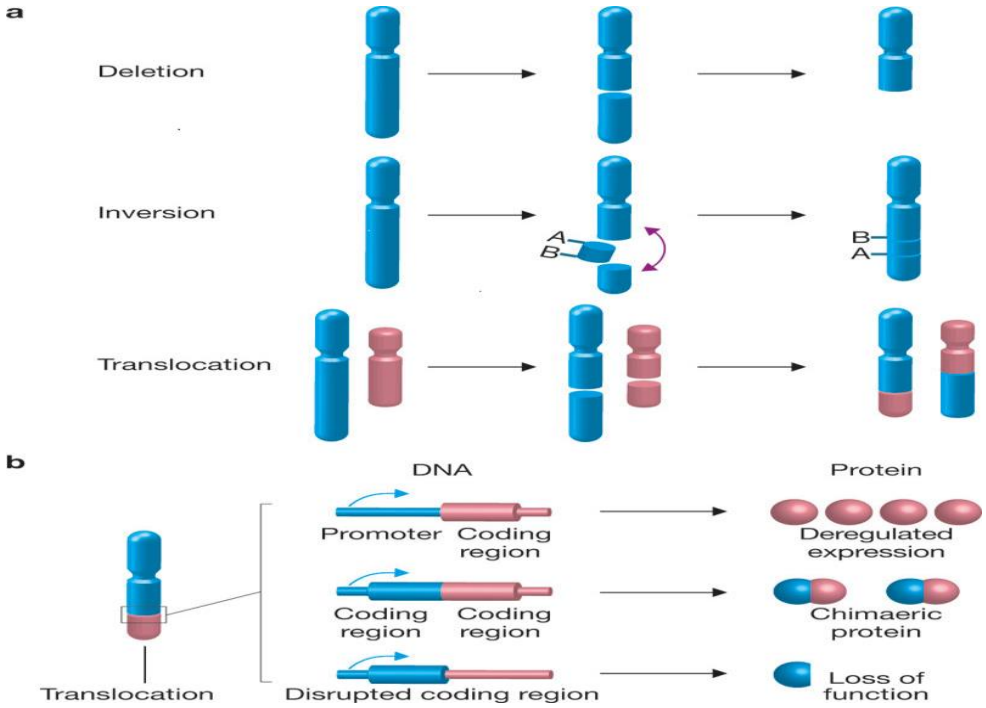

Figure 5 Formation of a chromosome translocation [23].

Furthermore, structural abnormalities can cause a range of health issues in the baby, depending on the location and size of the abnormality [20]. In some cases, chromosomal abnormalities may not be detected until after the baby is born [22].

The most common example is a Robertosonian translocation, which results when two acrocentric chromosomes (i.e., chromosomes with arms of unequal lengths due to a non-centered centromere) lose the short arms of the chromosomes, and the two long arms consequently conjoin. Robertsonian translocations are one potential cause of trisomies [20]. Notably, trisomy 21, or the presence of an extra chromosome 21, is the cause of Down syndrome [23]. Down syndrome is a genetic disorder caused by the presence of extra copies of chromosome 21. It can be either familial (caused by translocations) or sporadic (caused by (i) meiotic non-disjunction before fertilization or (ii) somatic non-disjunction after fertilization, i.e., mosaicism). Down syndrome can present with a variety of signs and symptoms, including brushfield spots, which are small white/grey spots on the edge of the iris, the colored part of the eye; dysmorphic features (e.g., atypically small head or flat face); gastrointestinal problems (e.g., vomiting); cardiovascular problems; neuromuscular problems (e.g., decreased muscle tone); pale skin; fatigue; and shortness of breath. The other two most common autosomal trisomies are trisomy 18, which results in Edwards syndrome, and trisomy 13, which leads to Patau syndrome [20] (Table 1 & Table 2). Edwards syndrome often presents with severe mental disability, clenched hands, a large back of the head, a small mouth, low-set ears, and rocker-bottom feet, which are characterized by large heels. Signs of patau syndrome include severe intellectual disability, a small head, small eyes, cleft lips or palate, more than five fingers on a hand (i.e., polydactyly), rocker-bottom feet, and malformation of the forebrain (i.e., holoprosencephaly). Advanced maternal age is a risk factor for all three trisomy disorders and for chromosomal aberrations in general.

However, advancements in prenatal testing have made it possible to detect some chromosomal abnormalities during pregnancy [24]. This allows expecting parents to make

informed decisions about their pregnancy and prepare for potential health concerns for their baby.

2.1 Clinical Features

The clinical features of structural chromosomal anomalies can vary widely, depending on the affected genes. However, some standard features include Developmental delay, Intellectual disability, Dysmorphic features, Birth defects, and Medical problems [25].

3. Aetiology of Chromosomal Abnormalities

The aetiology of chromosomal abnormalities is a complex and diverse topic, with various factors playing a role in their development. One of the leading causes of chromosomal abnormalities is errors during cell division [25, 26]. Chromosomes are responsible for carrying genetic information, and any mistakes or abnormalities in their structure can lead to abnormalities in the genetic code [25, 26]. This can happen during meiosis, where the chromosomes divide and mix genetic material during the formation of reproductive cells. During this process, errors can result in abnormal cell formation, leading to conditions such as Down syndrome, Turner syndrome, and Klinefelter syndrome [27].

Another significant factor in the aetiology of chromosomal abnormalities is exposure to harmful substances or environmental factors [28-30]. These can include radiation, asbestos (naturally occurring mineral fibres), toxins, and certain medications like marijuana and ecstasy. Exposure to these substances can cause damage to the genetic material, leading to abnormalities in the chromosomes [28-30]. For example, studies have shown a link between exposure to radiation, pesticides, industrial emissions, asbestos, heavy metals and an increased risk of chromosomal abnormalities, particularly in the developing fetus [28, 31, 32]. Notably, classes of naturally occurring mineral fibers that have been extensively utilized in industrial processes and products and are linked to harmful effects on human reproductive health are collectively referred to as asbestos [32]. Asbestos fibers are used in commercial and industrial settings because of their strength, flexibility, resistance to heat and electricity, and other qualities. Cement, insulating materials, and vehicle brakes are a few things that might contain asbestos. Because of their microscopic size and fibrous nature, the mineral fibers can be handled and released into the air, where they can be inhaled and cause respiratory illnesses by accumulating in the lungs. Mesothelioma, asbestosis, lung cancer, and aneuploidy are just a few of the harmful health outcomes linked to asbestos exposure [32]. Aneuploid gametes resulting from asbestos exposure can be caused by a variety of factors, including errors during mitosis or meiosis [32]. Errors during mitosis can lead to aneuploid gametes if the chromosomes are not appropriately separated during anaphase. Errors during meiosis can lead to the formation of aneuploid gametes if the chromosomes are not appropriately paired during synapsis or if the homologous chromosomes are not separated properly during anaphase I or II.

Aneuploidy can arise through various mechanisms, including chromosome non-disjunction during mitosis. In a study, aneuploidy formation in human bronchial epithelial cells exposed to asbestos has been investigated where asbestos exposure induced the formation of binucleated intermediates, cells with two nuclei that have not yet undergone cytokinesis. These binucleated intermediates underwent bipolar mitoses, which resulted in the formation of aneuploid daughter

cells. In addition, Zhang et al. [32] found that asbestos exposure can also induce multipolar mitosis formation, which further contributes to aneuploidy formation. These results suggest that chromosome non-disjunction during bipolar mitoses of binucleated intermediates and multipolar mitoses are significant mechanisms of aneuploidy formation in asbestos-exposed cells [32]. Mesothelial cells absorb asbestos fibers, disrupting mitotic spindles and influencing the cell cycle. Tangling asbestos fibers with mitotic spindles can cause chromosomal structural anomalies and mesothelial cell aneuploidy.

In some cases, chromosomal abnormalities can also be inherited from parents [33, 34]. Inherited chromosomal abnormalities can also occur due to consanguineous marriages, where parents share a common ancestor, increasing the likelihood of passing on genetic mutations [35].

Advancements in medical technology have highlighted the impact of advanced maternal age on the incidence of chromosomal abnormalities in offspring [36, 37]. As women delay childbearing, the prevalence of advanced maternal age is increasing globally. With age, the quality of a woman's eggs naturally declines, resulting in an elevated risk of chromosomal errors during cell division. This increased risk is particularly evident in conditions like Down, Edwards, Patau, Turner, and Klinefelter syndrome. Conversely, young maternal age (less than 20 years at conception) is less common but also associated with a slightly elevated risk of specific chromosomal abnormalities [36, 37]. This may be attributed to factors such as immature reproductive organs, hormonal imbalances, increased exposure to environmental toxins during adolescence, and genetic variations that affect chromosome segregation during meiosis. Specific abnormalities associated with young maternal age include Trisomy 16, 22, and Monosomy X (Turner syndrome) [36, 37].

The connection between lifestyle factors and chromosomal abnormalities in pregnancy is becoming an increasingly relevant and vital area of research [38]. Over the past few decades, there has been a growing interest in the role of lifestyle factors in the etiology of chromosomal abnormalities in pregnancy. One particular area of research is focused on the influence of nutrition and diet on chromosomal abnormalities in pregnancy. Studies have shown that nutritional deficiency in pregnant women, specifically diets low in folate, vitamins B6 and B12, choline, betaine, methionine, thiamine, riboflavin, zinc, and other essential micronutrients, can increase the risk of chromosomal abnormalities in the fetus [39]. Studies suggest that deficiency in these essential micronutrients not only increases the risk of chromosomal abnormalities in the fetus but also can increase the risk of congenital malformations and low birth weight [40]. Additionally, nutritional deficiencies were linked to a variety of other conditions, such as diabetes, viral hepatitis, and hypertension. However, metabolic disorders and hepatitis B virus infection have been linked with an increased risk of fetal chromosomal abnormalities [41, 42].

In addition to nutrition, various studies have examined the effect of lifestyle factors such as smoking, alcohol consumption, and drug intake on the development of chromosomal abnormalities in unborn babies.

Smoking is one of the most commonly reported lifestyle factors associated with chromosomal abnormalities in pregnancy [43]. Research has found that women who smoke during pregnancy are more likely to have a baby with a chromosomal abnormality than those who do not smoke [44, 45]. Nicotine, tar, and other toxic substances found in cigarette smoke increase the risk of chromosomal abnormalities [44]. These toxins can damage the developing baby’s cells, leading to chromosomal abnormalities, and can also affect egg and sperm development, leading to an

increased risk of chromosomal abnormalities. Studies suggest that smoking during pregnancy can cause an increased risk of fetal malformations, chromosomal abnormalities, and miscarriage [43].

Alcohol consumption is another lifestyle factor associated with chromosomal abnormalities in pregnancy. Numerous studies have shown that drinking alcohol during pregnancy increases the risk of chromosomal abnormalities in the unborn baby [46]. Alcohol can interfere with the development of the fetus's cells, leading to chromosomal abnormalities. Furthermore, alcohol consumption during pregnancy can limit the availability of essential nutrients to the developing baby, leading to an increased risk of chromosomal abnormalities. Alcohol consumption during pregnancy can also increase the risk of chromosomal abnormalities, as well as other issues such as fetal alcohol syndrome, growth retardation, and malformations [47, 48]. Fetal Alcohol Syndrome (FAS) is a group of birth defects that occur in children whose mothers drink alcohol during pregnancy. These defects can range from mild to severe and affect the child's physical, mental, and behavioral development. Alcohol can cross the placenta and reach the fetus, where it can disrupt fetal development. Alcohol can cause several problems in the fetus, including;

- Growth retardation: Alcohol can restrict the growth of the fetus, leading to low birth weight and stunted growth.
- Facial abnormalities: Alcohol can cause facial abnormalities in the fetus, such as a flattened nasal bridge, small eyes, and a thin upper lip.
- Intellectual disabilities: Alcohol can damage the developing brain of the fetus, leading to intellectual disabilities such as learning difficulties, memory problems, and attention deficit hyperactivity disorder (ADHD).
- Behavioral problems: Alcohol can also lead to behavioral problems in children, such as aggression, hyperactivity, and difficulty controlling impulses.

Obesity and Cytomegalovirus infection are both risk factors for gestational diabetes, a condition that can lead to fetal macrosomia (excessive birth weight) and others. Obesity is a condition characterized by excessive body fat that increases the risk of health problems. It is caused by Genetic factors, unhealthy diet, physical inactivity, and certain medical conditions (e.g., hypothyroidism). Obesity increases the risk of preeclampsia, a condition characterized by high blood pressure and protein in the urine. Obesity can increase the risk of CMV infection during pregnancy. Cytomegalovirus (CMV) is a common virus that can cause symptoms from mild to severe. It can be spread by contacting infected bodily fluids (e.g., saliva, urine). CMV infection during pregnancy can cause congenital CMV in the fetus, which can have severe health consequences. Obesity and CMV infection can both contribute to fetal macrosomia, which can lead to complications during labor and delivery. MV infection can worsen the health risks associated with obesity, such as gestational diabetes and preeclampsia.

Toxoplasmosis is an infection caused by the parasite Toxoplasma gondii. It can be transmitted to humans through contact with infected cat feces, raw or undercooked meat, or contaminated water. Toxoplasmosis can have severe consequences for pregnant women and their unborn babies. If a pregnant woman becomes infected with Toxoplasma, the parasite can cross the placenta and infect the fetus. This can lead to miscarriage, stillbirth, or congenital toxoplasmosis in the newborn. Congenital toxoplasmosis can cause a range of health problems in infants, including Brain damage, Eye infections, Seizures, and Intellectual disability. There is no vaccine to prevent toxoplasmosis in humans. However, pregnant women can take steps to reduce their risk of infection, such as:

- Avoiding contact with cat feces
- Washing fruits and vegetables thoroughly
- Cooking meat thoroughly

4. Prevalence of Chromosomal Abnormalities in Pregnancy

The prevalence of chromosomal abnormalities in pregnancy is a topic of great concern for expecting parents and healthcare professionals alike. In this review, we will explore the current research and statistics on the prevalence of chromosomal abnormalities in pregnancy. According to Li et al. [49], chromosomal abnormalities are the leading cause of pregnancy loss and birth defects in the United States. It is estimated that 1 in every 200 pregnancies is affected by a chromosomal abnormality [49]. This equates to approximately 0.5% of all pregnancies. While this may seem like a small percentage, it is still significant, considering the number of pregnancies that occur each year.

The most common chromosomal abnormality in pregnancy is Down syndrome, also known as trisomy 21 [17-19]. This condition occurs when a person has an extra copy of chromosome 21, resulting in intellectual and developmental disabilities. According to the study carried out by De Graaf et al. [50], about 1 in every 700 babies in the United States is born with Down syndrome. This means that Down syndrome accounts for about 50% of all chromosomal abnormalities in pregnancy.

Other common chromosomal abnormalities include trisomy 18 and trisomy 13, which occur in about 1 in every 5,000 live births [51]. These conditions are more severe than Down syndrome and often result in stillbirth or death shortly after birth [51]. Turner syndrome, which affects only females, occurs in about 1 in every 2,500 live births. This condition is characterized by short stature and infertility [52]. Klinefelter syndrome is a genetic disorder caused by an extra X chromosome in males, resulting in the karyotype 47, XXY. During cell division, an error occurs in separating sex chromosomes and forming sperm or eggs with an extra X chromosome. When such sperm fertilizes an egg with a normal X chromosome, a child with Klinefelter syndrome is born with various symptoms such as tall stature, Gynecomastia, small testes, attention deficit hyperactivity disorder (ADHD), learning difficulties, infertility, etc. Klinefelter syndrome is relatively common, affecting about 1 in 500 males. It is usually diagnosed during childhood or adolescence, but it can sometimes go undiagnosed until adulthood.

The prevalence of chromosomal abnormalities in pregnancy also varies based on maternal age. As women age, the risk of having a baby with a chromosomal abnormality increases [36, 37]. According to the American College of Obstetricians and Gynecologists, the risk of having a baby with Down syndrome at age 35 is about 1 in 350. In contrast, at age 45, the risk increases to 1 in 30.

5. Diagnostic Testing for Chromosomal Abnormalities

Diagnostic testing for chromosomal abnormalities in pregnancy is an essential tool for identifying potential genetic issues in an unborn baby (Table 3). These tests are usually recommended for pregnant women who are at a higher risk for chromosomal abnormalities, such as women over the age of 35 or those with a family history of genetic disorders.

Table 3 Prenatal testing techniques for chromosomal abnormalities.

References	Test	Method	Timing	Accuracy	Risk
[30, 53]	Amniocentesis	Amniotic fluid is collected from the uterus and tested for chromosomal abnormalities	15-20 weeks of gestation	99.9%	Miscarriage (0.5%) Infection Bleeding cramping Rh sensitization (in Rh-negative mothers)
[54, 55]	Chorionic Villus Sampling (CVS)	Chorionic villi (part of the placenta) are collected and tested for chromosomal abnormalities	10-13 weeks of gestation	99.9%	Miscarriage (1%) Infection Bleeding Rh sensitization (in Rh-negative mothers)
[56]	Non-Invasive Prenatal Testing (NIPT)	A blood sample from the mother is tested for fetal DNA, which can be used to screen for chromosomal abnormalities	10 weeks of gestation	99% for Down syndrome, 96% for Edwards syndrome, 92% for Patau syndrome	False positives (0.5-2%) False negatives (0.1%)
[53]	Ultrasound	High-frequency sound waves are used to create images of the fetus	18-20 weeks of gestation	80-90% for significant chromosomal abnormalities	None
[53]	Fetal Echocardiogram	A detailed ultrasound of the fetal heart	18-20 weeks of gestation	95% for major heart defects	None

One of the most common diagnostic tests for chromosomal abnormalities is amniocentesis [53]. This procedure involves inserting a thin needle through the mother's abdominal wall and into the uterus to collect a sample of amniotic fluid from the amniotic sac (Figure 6), which surrounds the developing fetus [30]. The amniotic fluid contains fetal cells that can be analyzed for chromosomal abnormalities, such as Down syndrome, trisomy 18, and neural tube defects. The procedure is usually guided by ultrasound to ensure the safety of the fetus. This test is generally performed between 15 and 20 weeks of pregnancy and has a high accuracy rate [53]. The collected sample is then sent to a laboratory for testing, and results are typically available within two to three weeks. The risk of miscarriage is small, but it is slightly higher than the risk associated with other prenatal tests. Amniocentesis can introduce infection into the uterus, which can be harmful to both the mother and the baby. Amniocentesis can cause bleeding and cramping, which can be uncomfortable.

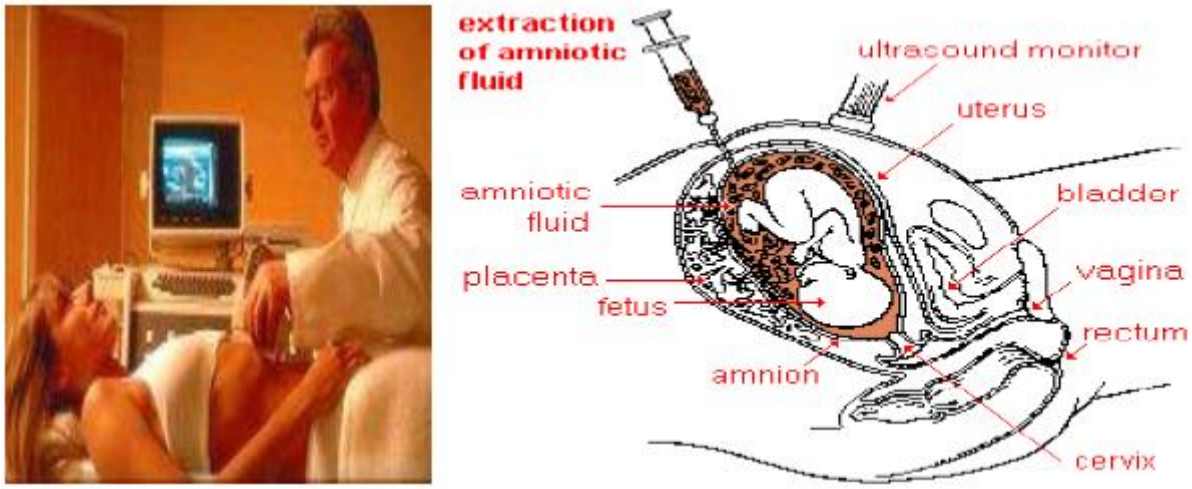

Figure 6 Extraction of an amniotic fluid sample.

Another standard diagnostic test is chorionic villus sampling (CVS) [54, 55]. This test involves taking a sample of cells from the placenta, which can also be analyzed for chromosomal abnormalities. CVS can be performed earlier in pregnancy, usually between 10 and 13 weeks, but it does carry a slightly higher risk of miscarriage compared to amniocentesis [54, 55].

A newer non-invasive prenatal screening test (NIPT) has recently become available for detecting chromosomal abnormalities. This test involves analyzing a sample of the mother's blood for fetal DNA [56]. It is a simple and safe test that can be done as early as 10 weeks of pregnancy. However, NIPT is not a diagnostic test and is usually followed up with amniocentesis or CVS for confirmation. These diagnostic tests can detect various chromosomal abnormalities, including Down syndrome, Turner syndrome, and trisomy 18. If the parents are known carriers, they can detect specific genetic disorders, such as cystic fibrosis or sickle cell disease [56]. The results of these tests can provide valuable information for expecting parents. If a chromosomal abnormality is detected, parents can make informed decisions about their pregnancy and prepare for the future care of their child. They may also choose to undergo additional testing or seek genetic counseling to understand the diagnosis's implications better.

Overall, there is evidence linking chromosomal anomalies to repeated miscarriages at the parent, gamete, and fetal levels. Abnormalities in numbers and structure provide the most compelling evidence of a connection to the illness.

Repeated miscarriages, defined as the loss of three or more consecutive pregnancies, can be a devastating experience. While numerous factors can contribute to this, chromosomal abnormalities play a significant role, often stemming from issues related to sperm DNA integrity [57]. Here's a breakdown of the key concepts:

Chromosomal Abnormalities Linked to Repeated Miscarriages through Sperm DNA Fragmentation [57]:

1. **Causes:** Sperm DNA fragmentation refers to the breakage or damage in the DNA within sperm cells. This can be caused by various factors, including:
   Lifestyle Factors: Smoking, alcohol consumption, exposure to environmental toxins, and even stress can contribute to DNA damage.

Age: As men age, their sperm quality deteriorates, increasing the risk of DNA fragmentation.

Medical Conditions: Certain conditions like varicocele (enlarged veins in the scrotum) and infections can also impact sperm DNA integrity.

Oxidative Stress: This can damage sperm DNA and is linked to factors like smoking, obesity, and radiation exposure.

Consequences: Fragmented DNA in sperm can lead to:

Failed fertilization: Damaged DNA might prevent the sperm from successfully fertilizing the egg.

Embryonic arrest: Due to the damaged genetic material, the embryo may stop developing.

Miscarriage: The developing fetus may be unable to survive due to significant genetic abnormalities.

Diagnosis: Sperm DNA fragmentation can be tested through various methods, such as the TUNEL (Terminal deoxynucleotidyl transferase dUTP nick end labeling) assay or the SCSA (Sperm Chromatin Structure Assay) test.

2. Telomere Length and Aneuploidy Formation:
   Telomeres are protective caps at the ends of chromosomes that play a crucial role in cell division and stability. They shorten with each cell division, and their length is linked to aging and disease. Shortened telomeres have been associated with an increased risk of aneuploidy. This is because shorter telomeres can make chromosomes more susceptible to breakage and mis-segregation during cell division, leading to an abnormal number of chromosomes in the resulting cells [57]. Aneuploidy in embryos can lead to miscarriage, birth defects, and developmental problems.
3. Skewed X-Inactivation as a Surrogate of Mosaicism and Related Conditions:
   One of the two X chromosomes in females is inactivated randomly in each cell. This is known as X-inactivation or Lyonization. Sometimes, one X chromosome is preferentially inactivated over the other, leading to a skewed inactivation pattern. This can be a surrogate marker for mosaicism [57]. Mosaicism refers to two or more genetically distinct cell populations within an individual. It can arise from mutations occurring during early embryonic development. Skewed X-inactivation can be associated with various conditions, including Turner Syndrome and X-linked Diseases like Duchenne muscular dystrophy.

   Overall, Understanding the complex interplay between chromosomal abnormalities, sperm DNA fragmentation, telomere length, and X-inactivation is crucial for addressing the challenges of repeated miscarriages. By investigating these factors, clinicians can better identify potential causes, offer appropriate interventions, and provide personalized guidance to couples experiencing this difficult situation.

6. Insight into Developing Strategies for Reducing and Preventing Chromosomal Abnormalities in Pregnancy

Chromosomal abnormalities are a significant contributor to adverse pregnancy outcomes, including spontaneous abortions, stillbirths, and severe birth defects. A comprehensive strategy for reducing chromosomal abnormalities in pregnancy should, therefore, be part of

comprehensive strategic Psychological services, drug therapy, exercise therapeutic strategy, hormonal therapeutic strategy, and nutritional therapeutic strategy.

6.1 Psychosocial Services

Psychosocial services are essential support systems for expectant parents facing chromosomal abnormalities in their pregnancy [58]. This includes access to genetic counseling, psychological support, and support for the mother, baby, and family [58]. These services provide resources, information, and counseling to expectant parents and their families during difficult times. Through psychosocial services, the family is allowed to develop a coping plan and manage complex issues related to the diagnosis of chromosomal abnormalities. Pre-conception counseling can provide individuals with valuable information about their risk of having a child with a chromosomal abnormality. It can help them make informed decisions about their reproductive health [58].

6.2 Drug Therapies for the Management of Chromosomal Abnormalities in Pregnancy

The management of chromosomal abnormalities in pregnancy is a complex and emotionally fraught endeavor that requires a comprehensive approach involving all the medical disciplines relevant to monitoring and managing the condition. While the technology to diagnose many genetic conditions has come a long way in recent years, managing and treating these conditions often remain challenging. Many conditions may require a customized care plan tailored to the individual patient, her family, and the specific chromosomal abnormality identified. This is to ensure that the best possible outcome is achieved.

Buprenorphine is a partial opioid agonist. It is used to treat opioid dependence or opioid use disorder (OUD). Despite its clinical utility and safety in treating opioid dependence and improving the health of pregnant women and their babies during pregnancy, Buprenorphine can also cause nausea, vomiting, and constipation (Table 4). There is also a potential risk of neonatal abstinence syndrome, such as tremors, jitteriness, and irritability, which can occur when the baby is born after exposure to opioids. More so, Buprenorphine can cause respiratory depression in newborns. Although, the benefits of Buprenorphine in pregnancy generally outweigh the risks. Suarez et al. [59] conducted a retrospective cohort study using data from publicly insured Medicaid beneficiaries in the US from 2000 to 2018 to assess the risk of congenital malformations in infants born to 9514 pregnant women who used Buprenorphine or 3846 pregnant methadone during the first trimester of pregnancy. According to Suarez et al. [59], the overall risk of malformations was 50.9 per 1000 pregnancies for Buprenorphine and 60.6 per 1000 pregnancies for methadone. After adjusting for confounding factors, Buprenorphine was associated with a lower risk of malformations than methadone (RR: 0.82; 95% CI: 0.69-0.97). Buprenorphine was associated with a lower risk of specific malformations, including:

- Cardiac malformations (RR: 0.63; 95% CI: 0.47-0.85)
- Ventricular septal defect (RR: 0.62; 95% CI: 0.39-0.98)
- Secundum atrial septal defect/non-prematurity-related patent foramen ovale (RR: 0.54; 95% CI: 0.30-0.97)
- Oral clefts (RR: 0.65; 95% CI: 0.35-1.19)
- Clubfoot (RR: 0.55; 95% CI: 0.32-0.94)
- Results for neural tube defects were uncertain due to low event counts.

- In secondary analyses, Buprenorphine was associated with:
- Decreased risk of central nervous system, urinary, and limb malformations
- Increased risk of gastrointestinal malformations compared to methadone
- Sensitivity and bias analyses supported the main findings.

Whereas Infants exposed to methadone during the first trimester had an increased risk of:

- Neonatal abstinence syndrome (aOR: 29.21)
- Short stature (aOR: 1.56)
- Clubfoot (aOR: 1.50)
- Omphalocele (aOR: 1.89)
- Anorectal atresia (aOR: 2.40)

Table 4 Indications, side effects, and benefits/costs ratio of medications used in pregnancy.

Medication	Indications	Side effects	Benefits/Costs Ratio
Buprenorphine	opioid use disorder (OUD)	Nausea, vomiting, constipation, sweating, sleep disturbances, mood changes	Improved maternal and fetal outcomes; potential risks of neonatal abstinence syndrome
Naltrexone	opioid use disorder (OUD)	Nausea, vomiting, diarrhea, sweating, sleep disturbances	Reduced risk of relapse; potential risks of pregnant termination
Methadone	opioid use disorder (OUD)	Nausea, vomiting, constipation, sweating, sleep disturbances, mood changes	Improved maternal and fetal outcomes; potential risks of neonatal abstinence syndrome
Fluoxetine	Depression, anxiety	Nausea, vomiting, diarrhea	Improved maternal mental health; potential risks to fetal development

Additionally, there was an 18% decrease in relative risk for malformations overall, which equates to 1 less occurrence per 100 pregnant individuals treated with buprenorphine [59]. Notably, the risk of congenital malformations was significantly higher in infants exposed to methadone than in infants exposed to Buprenorphine. These findings emphasize the importance of optimizing prenatal care and providing comprehensive counseling to women using these medications during pregnancy. More so, several alternative treatments for depression and opioid dependence can be used during pregnancy. These include Psychotherapy, Acupuncture, yoga, behavioral therapy, and exercise. The decision of which treatment to use during pregnancy should be made on a case-by-case basis in consultation with a healthcare provider.

In addition, the use of medication during pregnancy has become a significant concern for both patients and their healthcare providers. The safety of the developing fetus is of utmost importance, and the use of SSRIs (selective serotonin reuptake inhibitors) during pregnancy has been a particularly problematic issue. These drugs have been linked to a range of potential risks for the developing fetus, including miscarriage, premature delivery, neonatal complications, birth defects (especially cardiac defects), and more recently [28], neurodevelopmental disorders in

childhood, such as autism spectrum disorders. A study has examined the effects of individual SSRIs, and while the risk is small, there appears to be a slightly higher risk of birth defects. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) antidepressant. It is used to treat depression, obsessive-compulsive disorder, panic disorder, bulimia nervosa, and premenstrual dysphoric disorder. It is generally considered safe for use during pregnancy, but it can cause nausea, vomiting, and diarrhea. There is also a potential risk of fetal developmental problems, such as heart defects and cleft lip, in pregnant women with depression treated with fluoxetine [28]. It can also cause neonatal withdrawal symptoms, such as tremors, jitteriness, and irritability. However, fluoxetine can help to improve the mental health of pregnant women and reduce the risk of postpartum depression. Furthermore, research strongly suggests that the brain changes associated with Down syndrome begin in utero, emphasizing the importance of early intervention. This early window of opportunity, stretching from prenatal diagnosis to the 28th week of gestation, presents a unique chance to influence brain development and enhance cognitive outcomes positively. While research is ongoing, several promising therapeutic strategies such as Apigenin, Fluoxetine, NAP/SAL, and Epigallocatechin Gallate have been explored in animal models, demonstrating potential benefits for aneuploidy like Down syndrome [60]. However, the benefits of fluoxetine in pregnancy generally outweigh the risks. Notably, deciding whether to take fluoxetine during pregnancy should be made on a case-by-case basis.

6.3 Nutritional Therapeutic Strategies

Nutrition is vital in maintaining a healthy pregnancy [61, 62]. Certain nutrients have been shown to benefit chromosomal health (Table 5), such as folate, omega-3 fatty acids, magnesium, zinc, and vitamin D [39-42].

Table 5 Different nutrients, sources, benefits, and possible side effects.

Nutrient types	Sources	Benefits	Recommended dosage	Side effects
Vitamin D (cholecalciferol)	Fatty fish and fortified foods; skin through sun exposure	muscle, immune, nervous, and cardiovascular functions. The most active form of vitamin D, 1,25-dihydroxyvitamin D, increases intestinal absorption of calcium and bone resorption and reduces the renal excretion of calcium and phosphate. It reduces the risk of chromosomal abnormalities	30 to 100 ng/mL	Confusion, apathy, repeated vomiting, abdominal discomfort, polyuria, polydipsia, and dehydration
Vitamin E (tocopherol)	Nuts, soybeans, avocados, wheat, leafy vegetables, and olive oil.	Reduction in chromosomal damage in down syndrome patients. It protects the cell membrane and also acts as an antioxidant	15 mg/day	Hemorrhage, Muscle weakness and Gastrointestinal issues

Folate	green leafy vegetables such as cabbage, kale, spring greens and spinach, legumes, citrus fruits, meats, eggs, and milk	It prevents neural tube defects	400 mcg/d, with higher intakes (400-800 mcg/d) recommended during pregnancy to prevent neural tube defects	Gastrointestinal distress (Nausea, diarrhea, and abdominal cramps), Kidney stones (Increased risk of kidney stone formation), Iron overload
Zinc	fish, oysters, red meat, legumes, nuts, whole grains, and dairy	It reduces the risk of birth defects. It acts as a cofactor or structural modulator	10 mg/d	Immune System Dysregulation, Gastrointestinal Issues (nausea, vomiting, diarrhea, and abdominal cramps)
Omega-3 fatty acids		It reduces the risk of structural and genetic abnormalities	1.4-1.6 mg/d	as fishy taste, eructation, dyspepsia, diarrhea, gas, nausea, and arthralgia
Magnesium	fruits, vegetables, whole grains, legumes, nuts, dairy, and meat	It reduces the risk of preterm birth and cerebral palsy in infants with chromosomal abnormalities, such as Down syndrome. It's responsible for energy transfer, metabolism, bone development, and neuromuscular function	400 mg/d	Mild effects: muscle weakness and fatigue, Nausea and vomiting, Diarrhea, Headache, Drowsiness More severe cases are presented with Hypotension, Cardiac arrhythmias, Respiratory depression, Paralysis, and Coma

Folate, or vitamin B9, is a necessary component for DNA replication and serves as a substrate for several enzymatic processes related to the production of amino acids and the metabolism of vitamins. Pregnancy raises the demand for folate because the developing fetus also needs it for growth and development. A lack of folate has been linked to anomalies in fetuses (congenital abnormalities) and mothers (anemia, peripheral neuropathy) [39]. Hence, Foliate supplementation is an essential vitamin usually recommended for all pregnant women to help reduce the risk of neural tube defects in the fetus [39]. Folate supplementation before conception and during pregnancy has been found to reduce the risk of fetal chromosomal abnormalities, particularly when given in high doses. Folic acid is found in various foods, such as green leafy vegetables, legumes, and citrus fruits, and is often prescribed as a supplement. According to Hollis et al. [63] investigation, it was suggested that lack of folic acid supplementation may be explicitly associated with Meiosis II (MII) errors in the aging oocyte. MII errors refer to chromosomal abnormalities that

occur during the second meiotic division of the oocyte. These errors can result in aneuploidy, meaning the oocyte has an abnormal number of chromosomes.

Omega-3 fatty acids are found in fish and have been found to reduce the risk of structural and genetic abnormalities [64]. Moreover, researchers have established that consuming omega-3 fatty acids may also be beneficial for reducing the risk of chromosomal abnormalities in pregnant women [65].

Magnesium is a mineral that can be found in nuts and whole grains, and it has been found to reduce the risk of preterm birth [40]. Magnesium sulfate is an intravenous medication that has been used in pregnant women with preterm labor for more than 50 years. This medication is effective in reducing the risk of cerebral palsy in infants with chromosomal abnormalities, such as Down syndrome.

Also, one type of new plant-based medicine with many different medical uses is called arjunolic acid. Initially discovered in Terminalia arjuna and later found in Combretum nelsonii, Leandra chaeton, and other medicinal plants, this triterpenoid saponin offers a variety of therapeutic benefits [23]. A study has established that consuming arjunolic acids could attenuate the risk of chromosomal abnormalities in rats treated with flouxetine [28]. Arsenic is a metalloid in various forms in the environment, including inorganic and organic compounds. Exposure to arsenic can occur through contaminated drinking water, food, air, or occupational settings. Arsenic exposure has been associated with an increased risk of aneuploidy [66]. This can lead to developmental disorders, such as Down syndrome. It can induce chromosomal breaks and rearrangements, which can contribute to genomic instability and potentially lead to cancer. The mechanisms by which arsenic induces chromosomal abnormalities involve interference with DNA replication and repair, oxidative stress, and epigenetic alterations [66]. However, arjunolic acid has been shown to enhance the serum concentration of Vitamin B12 and Folate while mitigating uterine oxidative stress caused by arsenic exposure [67].

'NTDs (Neglected Tropical Diseases) are a group of preventable and treatable diseases prevalent in tropical and subtropical regions worldwide. They affect more than 1 billion people, primarily in low-income communities, and cause significant morbidity and mortality.' Hence, In a population-based case-control study conducted by Ellen et al. [41], maternal supplemental zinc intake could not be linked to the occurrence of NTDs. Cases were infants with NTDs born in California between 1989 and 1999, and Controls were infants without NTDs who were matched to cases by birth year, race/ethnicity, and maternal education. Nonetheless, a lower incidence of non-traumatic deaths was linked to mothers' dietary zinc consumption. Mothers who received the most excellent percentile of dietary zinc during pregnancy had a 25% lower risk of non-typing diarrhea (NTD) than mothers who ingested the lowest quintile. According to this study, a lower incidence of non-traumatic deaths (NTDs) was linked to maternal dietary zinc intake but not supplementary zinc intake. This research implies that dietary zinc intake may have a significant role in avoiding non-verbal developmental disorders (NDDs), particularly for women who are at high risk of producing a child with an NTD, such as those who have had a previous NTD or are taking specific drugs that may raise the risk of NTDs [41]. Zinc deficiency has increased DNA strand breaks [68], chromosomal instability, and aneuploidy in oocytes [69]. In Young's study [69], sperm disomy X (aneuploidy sperm) frequencies were reported to be 50% lower in men with high total zinc consumption compared to the moderate intake group ($P < 0.001$) and 39% lower in men with low intake ($P = 0.02$). For sperm disomy X, there was a significant trend throughout the intake

categories (P = 0.04). Though males with low total zinc intake had reduced frequencies of sex nullisomy compared with the moderate intake group (P = 0.03), there was no inverse relationship between total zinc intake and any other kind of sperm aneuploidy.

Vitamin: Vitamin D is important for strong bones and can be found in foods like eggs and fortified milk products (Figure 5). It has been found to reduce the risk of genetic abnormalities through its multifaceted effects on gene regulation, DNA repair, anti-inflammatory actions, epigenetic modifications, and cell cycle regulation. Ensuring adequate vitamin D intake through diet, sunlight exposure, or supplementation is crucial for maintaining genetic stability and overall health [39, 70]. Numerous studies have demonstrated the protective effects of vitamin D against genetic abnormalities: A human study showed that higher vitamin D levels were associated with a decreased risk of Down syndrome [71]. Another study linked low vitamin D levels in pregnant women to an increased risk of neural tube defects in their children [72]. Vitamin E (DL-alpha-tocopherol) has been reported to have a preventive effect against chromosomal damage in lymphocytes from Down syndrome (DS) patients as well as from controls [67]. G2 phase refers to a specific stage in the cell cycle, specifically the gap phase 2, after DNA replication (S phase) and mitosis (M phase). During G2, the cell prepares for cell division by synthesizing proteins and organelles necessary for mitosis. Chromosomal aberrations were observed during the G2 phase of the cell cycle, the stage immediately preceding mitosis. Thus, this was part of analyzing the rates of basal and G2 chromosomal aberrations in lymphocytes grown with and without 100 microM vitamin E. By counting the number of chromosomal abnormalities in lymphocyte cultures treated with 5 mM caffeine two hours before harvesting, the amount of chromosomal damage in G2 was ascertained. Vitamin E therapy reduced the basal and G2 chromosomal abnormalities in both the control and DS cells. This protective effect, which was seen as a reduction in chromosomal damage, was higher in DS cells (50%) compared to controls (30%) [73].

More so, from a study carried out by Young et al. [69], Vitamin C, vitamin E, and the antioxidant composite variable did not show any correlations with total intake or any measured sperm aneuploidy; however, men with high levels of total β-carotene (provitamin A) consumed had fewer disomy Y frequencies (4.0 versus 5.5, P = 0.03) and men with low levels (4.0 versus 5.6, P = 0.04) showed a significant trend (P = 0.04).

While vitamins are essential for health, it is crucial to consume them in moderation. By understanding the causes, symptoms, and prevention measures, individuals can minimize their risk of developing hypervitaminosis (excessive intake of specific vitamins) and maintain optimal health.

6.4 Fetal Blood Transfusion Strategies

Fetal blood transfusions are a procedure wherein blood is transfused from an umbilical cord to the fetus in utero to treat anemia caused by abnormal placental development [74]. This therapy is effective in treating anemia in fetuses with chromosomal abnormalities and can also reduce the risk of preeclampsia [75]. However, this therapy must be carefully monitored due to potential complications such as intrauterine infection, fetal-maternal hemorrhage, and traumatic delivery.

6.5 Reduction of Excess Intake of Sugar

Excessive intake of other drugs, like sugar, may also be harmful. For example, hormonal changes and insulin resistance might result from gestational diabetes, a disorder that affects pregnant women without a history of diabetes [76]. It can be managed by exercising and reducing sugar consumption [77]. Gestational diabetes can cause premature birth, development abnormalities, obesity, respiratory problems, and diabetes in the unborn child [78]. Since gestational diabetes has been linked with an increased risk of fetal chromosomal abnormalities [41, 42], reduction of excess sugar intake can also help to prevent fetal chromosomal abnormalities.

7. Conclusion

In conclusion, Chromosome breakage and mis-segregation are two common mechanisms that can lead to chromosome abnormalities. These abnormalities can have a significant impact on pregnancy and newborn health. Some preventive strategies can be used to reduce the risk of these abnormalities. By implementing these strategies, we can help to improve reproductive health and reduce the incidence of pregnancy loss, congenital birth defects, and intellectual disability.

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Author Contributions

OMO and RAR conceived and wrote the manuscript; OMO polished the manuscript; OGT, AJM, OAO and PEO revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Competing Interests

The authors declare no conflict of interest.

Data Availability Statement

All data relevant to the study are included in the article or uploaded as Additional files.

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