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IN DEPTH STUDY ABOUT CHROMOSOMAL NON-DISJUNCTION IN A BRIEF REVIEW

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ABSTRACT: Chromosomal non-disjunction is a pivotal error in cell division where chromosomes fall to separate properly during meiosis or mitosis, resulting in an abnormal number of chromosomes, the condition is known as aneuploidy. This phenomenon has significant consequences for human health, as it underpins several kinds of genetic disease, such as Downsyndrome, Turner syndrome and Klinefelter syndrome. Non-disjunction may occur during mitosis, Meiosis-I or meiosis-II and various factors influence how sister chromatids or homologous chromosomes segregate. Maternal age is a significant risk factor, spicily for neostick non-disjunction triggered by prolonged oocyte stoppage in Prophase-I. Additional causes environmental and genetic and epigenetic alterations in cohesinproteins. Non-disjunction can cause developmental issues, miscarriages, mosaicism and chromosomal instability in cancer. The diagnosis of aneuploidy has increased due to advances in diagnostic procedure such as Karyotyping, Fluorescence *in-situ* hybridization (FISH) and non-invasive prenatal testing. Preimplantation genetic testing (PGT) and genetic counselling provide at risk families with preventive measures. Despite advancement in understanding the molecular causes and effects treatment options remains limited. Continued study is needed to understand the complexity of non-disjunction and to determined appropriate treatment. The present research emphasizes on the molecular principles, causal variables and clinical effects of chromosomal non-disjunction forcing on its significant in medical genetics and reproduction. Improved awareness and diagnostic capabilities will improve patient care while providing in sighting into the future preventive and therapeutic treatments.

INTRODUCTION: Chromosomal non-disjunction is a fundamental genetic abnormality that occurs during cell division, resulting in abnormality in chromosomal distribution to other cells. The development of organisms, genetic integrity and the onset of different genetic disorder are all significantly impacted by this occur as. Chromosomes are uniformly divided into daughter cell during a typical cell division process in order to preserve the proper amount of chromosome.

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Non-disjunction, on the other hand upsets this balance, resulting in cell with and aberrant amount of chromosomes known as aneuploidy [1].

Non-disjunction can occur during either mitosis or meiosis. Meiosis is a type of cell division that generate gametes with half the normal number of chromosomes. Non-disjunction in meiosisis particularly essential as it can pass chromosomal defects to the following generations. When sister chromatid fell to segregate correctly during meiosis II or homologous chromosome fall to split during meiosis I. As a result, gametes may have and extra chromosome (n+1) or lake 1 entirely (n-1). When such gametes marge during fertilization the resulting zygote has an on unusual chromosomal structure.

In multicellular organism, non-disjunction is less frequent but essential during mitosis, which is responsible for tissue growth development and repair. Daughter cells with mismatched number of chromosomes are the result of mitotic non-disjunction, which happened when sister chromatid do not properly split during anaphase. This aberration can lead tomosaicism, a condition in which distinct cell in the same organism have diverse genetic characteristic, which is common in malignant tissues. Chromosome non-disjunction can have verity of serious effect. Non-disjunction occurrences during meiosis produces a number of genetic daises in humans. Down syndrome also known as trisomy is cause by and extra copy of chromosome 21 leading to in cognitive disability, unique facial traits and a higher risk of certain medical disorder. In a similar vein, turner syndrome causes short stature infertility and other developmental disorders in females, is cause by lack of one X chromosome (monosomy X). Additional condition is also associate with a non-disjunction including Edward syndrome and Klinefelter syndrome (XXY). The impact and character of these disease are determining by extra chromosomes involved as well as if the abnormality is cause by a missing or extra chromosome.

The underlying mechanisms of non-disjunction are complex and multifaceted. Improper chromosomal segregation can result from cohesion abnormalities between chromatids, abnormal kinetochore attachment, or errors in spindle apparatus construction [2]. A major risk factor for meiotic non-disjunction is also maternal age, especially during oogenesis (egg development). According to studies, as women get older, their meiotic machinery deteriorates, increasing the risk of chromosome separation errors. Other factors that have been linked to an increased risk of non-disjunction include genetic predispositions, environmental factors, and certain chemical exposures.

It is essential to identify and diagnose non-disjunction events, especially in prenatal care. Molecular methods like fluorescent in situ hybridization (FISH) and quantitative PCR, as well as sophisticated diagnostic tools like karyotyping, which visualizes the entire set of chromosomes, allow the detection of chromosomal abnormalities. Using maternal blood samples for non-invasive prenatal testing (NIPT) has also become a potent technique for identifying foetal aneuploidies [3]. These technologies enable parents and healthcare practitioners to make informed pregnancy management decisions, as well as give early interventions when possible.

Genetics, developmental biology, and medicine all require an understanding of chromosomal non-disjunction. The molecular mechanisms behind chromosome segregation have been uncovered by this field of study, which has also opened the door for possible treatments that could reverse or lessen the impact of chromosomal abnormalities. Future advances in genome editing technologies, such as CRISPR, and regenerative medicine provide promise in tackling some of the issues given by non-disjunction-related illnesses.

Mechanisms of Chromosomal Nondisjunction:

Meiosis I: Nondisjunction in Meiosis I is a fundamental cellular defect in which homologous chromosomes fail to split during anaphase I, resulting in the formation of gametes with aberrant chromosomal numbers. Meiosis I is the initial division of meiosis, in which two daughter cells are formed from homologous chromosomes, one from each parent. During metaphase I, homologous chromosomes align at the metaphase plate in pairs, with spindle fibres from opposite poles connecting to each homolog's kinetochores [4]. During anaphase I, the spindle fibres separate these chromosomes, guaranteeing that every daughter cell obtains one chromosome from every homologous pair. Nondisjunction, on the other hand, interferes with this mechanism and makes both homologous chromosomes go to the same pole. Consequently, one daughter cell gains an additional chromosome (n+1), while the other cell loses that chromosome (n-1).

In Meiosis I, a number of molecular mechanisms lead to nondisjunction. Cohesin dysfunction, a protein complex that keeps sister chromatids together and aids in homologous chromosome alignment, is one important contributing factor. Additionally, cohesin is essential for preserving the chiasmata, which are the sites where homologs cross across and generate tension for correct alignment. Homologs might not separate properly

if cohesin malfunctions or fails too soon. Inappropriate microtubule-kinetochores attachment is another significant cause. Segregation failures can result from mistakes like monotelic attachment, in which only one homolog is connected, or synthetic attachment, even though each homolog normally connects to spindle fibres from opposite poles during meiosis. In order to ensure that chromosomes are appropriately aligned and joined before proceeding to anaphase, the spindle assembly checkpoint (SAC), a monitoring mechanism, should rectify these attachment problems. Nondisjunction could occur, though, if the SAC malfunctions and the cell divides in spite of these mistakes [5].

Nondisjunction during Meiosis I has serious repercussions since it impacts all subsequent gametes generated in Meiosis II. Gametes that originate from the separation of sister chromatids during Meiosis II will carry the aberrant chromosomal numbers produced during Meiosis I. Two gametes will have an additional chromosome (n+1), whereas two others will not (n-1). If these aberrant gametes are fertilized, they produce embryos with aneuploidy, or an imbalance in chromosome number. Down syndrome (Trisomy 21), which occurs when an individual receives three copies of chromosome 21, and Turner syndrome (Monosomy X), which occurs when one X chromosome is missing, are two examples of disorders caused by such abnormalities [6]. The probability of nondisjunction, particularly in maternal meiosis, rises with age as cohesin and other proteins that stabilize chromosomal structures degrade over time.

Nondisjunction in Meiosis I results from defects in homolog separation induced by cohesin malfunction, spindle attachment faults, or checkpoint failure. Gametes are greatly affected by the mistake, which frequently results in chromosomal abnormalities that can have serious effects on development and health. Understanding this mechanism is critical for treating genetic diseases and devising therapeutic strategies [7].

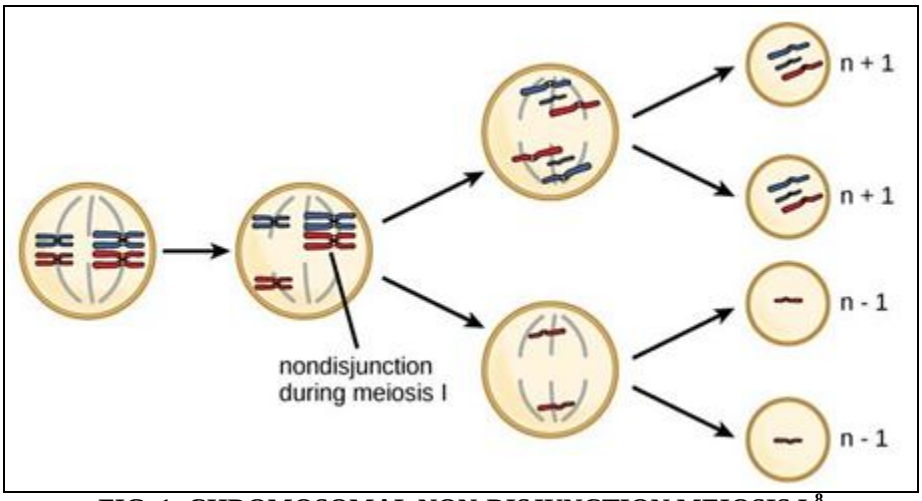

FIG. 1: CHROMOSOMAL NON-DISJUNCTION MEIOSIS I [8]

Meiosis II: Meiosis II's nondisjunction is a crucial mistake in sister chromatid segregation during gamete production that results in aneuploidy, or gametes with an abnormally high number of chromosomes. Meiosis II is the second division of meiosis, which occurs after homologous chromosomes have successfully separated during Meiosis I. During Metaphase II, each chromosome, which is made up of two sister chromatids, aligns with the metaphase plate. Spindle fibres adhere to the kinetochores of the sister chromatids, pulling them apart to opposing poles during anaphase II. Nondisjunction happens when sister chromatids are unable to separate properly. One daughter cell obtains both chromatids of a chromosome (n+1), whereas the other daughter cell receives none (n-1) as a result of both chromatids moving to the same pole rather than segregating into separate cells [9]. Normal haploid number (n) will be present in the other two gametes derived from the unaffected chromosomal group. Nondisjunction during Meiosis II is caused by a variety of processes. The failure of cohesin proteins, which ordinarily hold sister chromatids together until the appropriate

moment for separation, is a significant cause. Sister chromatids cannot separate and stay together if cohesin is not appropriately broken down during anaphase II. Another frequent reason is mistakes made in the way spindle microtubules adhere to the chromatid kinetochores. Microtubules from opposite poles must adhere to the kinetochores of sister chromatids in order to segregate normally. Proper segregation can be hindered by attachment mistakes, such as monotelic attachment, in which only one chromatid connects to spindle fibres, or syntelic attachment, in which both sister chromatids attach to microtubules from the same pole. The spindle assembly checkpoint (SAC), which ensures that all chromosomes are correctly aligned and linked to the spindle before progressing to anaphase, may also malfunction. Nondisjunction may result from the cell dividing with unresolved misalignments if the SAC fails to identify attachment faults [10]. Age-related factors also have a role, especially in female oocytes that are stopped in meiosis for long periods of time. Cohesin complexes lose their ability to sustain chromatid cohesion as their integrity deteriorates over time. This raises the probability of nondisjunction in older age groups of mothers. Nondisjunction in Meiosis II has a substantial impact on the chromosomal number in the resultant gametes. During fertilization, the zygote generated by these aberrant gametes may have trisomy or monosomy. Klinefelter syndrome (47, XXY), caused by an extra X chromosome, and certain cases of Down syndrome (trisomy 21), where the error occurs in the separation of chromosome 21 chromatids, are two examples of illnesses caused by nondisjunction in Meiosis II. Turner syndrome (45, X) can also occur if a gamete without an X chromosome contributes to the zygote. Nondisjunction in Meiosis II arises from a failure of sister chromatid separation caused by cohesin malfunction, spindle attachment problems, or checkpoint failure. This process alters the chromosomal balance in gametes, which has serious consequences for offspring health and development, emphasizing its importance in reproductive biology and genetics.

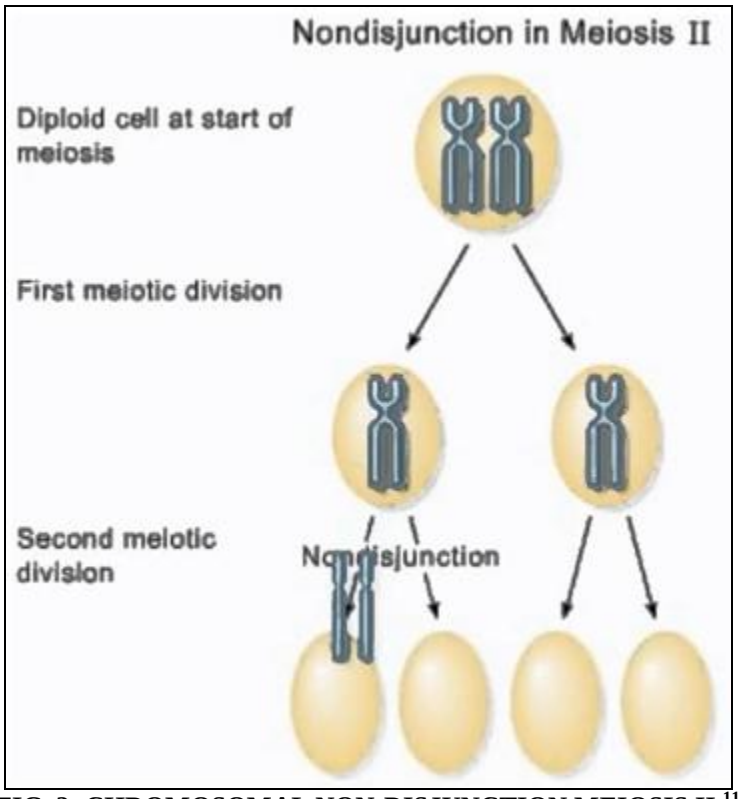

FIG. 2: CHROMOSOMAL NON-DISJUNCTION MEIOSIS II [11]

Mitosis: Nondisjunction in mitosis occurs when sister chromatids fail to separate properly during cell division, resulting in cells with aberrant chromosomal numbers, also known as aneuploidy. This error can happen during anaphase of mitosis, when the mitotic spindle typically pulls sister chromatids to the cell's poles. Mitosis is a vital mechanism in somatic cells that promotes

proliferation, tissue repair, and genetic stability. Many strictly controlled processes, such as spindle construction, microtubule attachment to kinetochores, and the timing of chromatid separation, are necessary for the correct segregation of sister chromatids [12]. When these mechanisms fail, nondisjunction can occur, altering the chromosomal balance in the offspring. The usual pattern is for one daughter cell to gain an extra chromosome (2n+1) and the other to lose a chromosome (2n-1). Such chromosome imbalances can result in mosaicism, which occurs when a population of cells within the same organism have different genetic makeup.

Mitotic nondisjunction is caused by a loss of normal spindle attachment to kinetochores, which are protein complexes found in chromosome centromeres. Spindle fibres from opposing poles must bind to sister chromatid kinetochores through a mechanism called amphoteric attachment in order for proper segregation to occur. Errors such as monotelic attachment, in which only one sister chromatid connects to the spindle, and merotelic attachment, in which one kinetochore attaches to spindle fibres from both poles, can cause faulty segregation. A crucial surveillance mechanism called the spindle assembly checkpoint (SAC) makes ensuring that chromosomes are properly positioned and joined to the spindle apparatus prior to the onset of anaphase. If the SAC fails or is overridden prematurely, the cell may go into anaphase despite attachment defects, resulting in nondisjunction [13].

Cohesin proteins, which maintain sister chromatids together along their lengths until anaphase, can malfunction, which is another major factor contributing to mitotic nondisjunction. Normally, cohesin is destroyed under regulated conditions during anaphase, allowing sister chromatids to split. Chromosomal segregation may be compromised if cohesin fails to breakdown correctly or is eliminated early [14]. Anaphase-promoting complex/cyclostome (APC/C) defects can also cause nondisjunction and interfere with mitotic progression. APC/C is a multiportion complex that starts chromatid separation. Furthermore, centrosome amplification or malfunction can result in the creation of multipolar spindles, which causes disorderly chromosomal segregation and increases the risk of aneuploidy.

In multicellular organisms in particular, mitotic nondisjunction has serious repercussions. Mitotic mistakes can cause aneuploidy, which can lead to illnesses like cancer, tissue malfunction, and problems in development. Chromosomal instability (CIN), which is frequently caused by mitotic nondisjunction in malignancies, creates genetic variability within the tumour cell population and accelerates tumour growth. Furthermore, mitotic nondisjunction in early embryonic development can cause mosaicism, in which some cells have normal chromosomal counts while others are aneuploid. Conditions like mosaic Down syndrome and some types of Turner syndrome are linked to mosaicism.

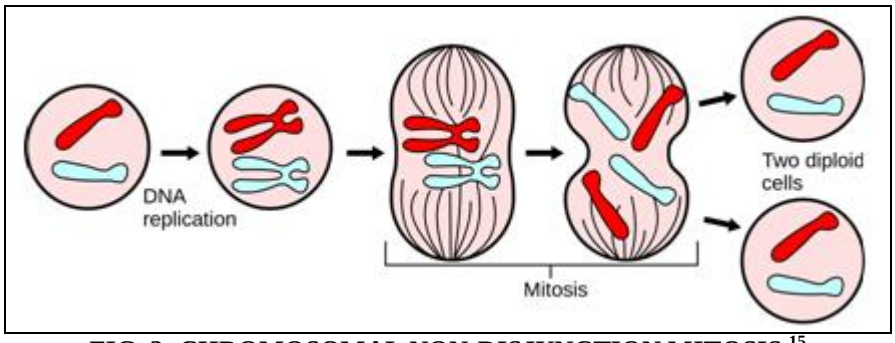

FIG. 3: CHROMOSOMAL NON-DISJUNCTION MITOSIS [15]

Causes of non-disjunction:

Age-Related Factors:

Maternal Age-Related Factors: Maternal age is a significant factor determining the probability of chromosomal non-disjunction, particularly in oocytes. Women are born with a limited number of oocytes that are stalled in prophase I of meiosis until ovulation. These oocytes undergo a protracted arrest as the mother ages, which results in a decline in both structure and function. The breakdown of

cohesin proteins, which are required to keep sister chromatids together, is an important factor. Cohesins diminish with age, increasing the risk of early chromatid separation. Similarly, age-related alterations in the spindle machinery, which is responsible for chromosomal alignment and segregation, can lead to incorrect chromosome segregation. Hormonal variations, such as lower oestrogen levels, might further destabilize the meiotic environment, increasing mistakes. The combined effect of these factors considerably increases the chance of aneuploidy, particularly trisomies, such as Down syndrome. According to statistical statistics, aneuploidy rates sharply increase after the age of 35 for mothers, highlighting the effect of aging on chromosomal integrity [16]. In order to reduce the hazards associated with delayed parenthood, it is crucial to understand these maternal age-related mechanisms and the advancements in reproductive technologies.

Paternal Age-Related Factors: Paternal age influences chromosomal non-disjunction and associated genetic disorders in a less obvious but still significant way. In contrast to oocytes, sperm are continuously created by a process called spermatogenesis; however, as people age, this process becomes less effective. One major reason is the accumulation of DNA damage caused by increased oxidative stress and diminishing DNA repair systems in elderly males. Chromosome instability may result from this damage, but nondisjunction is not the primary result. Moreover, sperm mutations and structural abnormalities are more common in older individuals, which may have an indirect impact on chromosome segregation during meiosis [17].

Despite being uncommon, paternal non-disjunction can result in sex chromosomal aneuploidies and disorders such Klinefelter syndrome (XXY). The longer time of spermatogenesis in older men raises the possibility of chromosomal pairing and segregation mistakes. Furthermore, studies indicate that the efficacy of cellular checkpoints that promote proper chromosome segregation may decrease with age, allowing errors to persist. Smoking, alcohol consumption, and exposure to environmental contaminants can exacerbate these consequences, increasing the risk. Understanding the parameters connected to paternal age is essential for genetic counselling and evaluating the reproductive risks associated with advanced paternal age, even though males are less likely than women to experience nondisjunction.

Genetic and Epigenetic Influences: In older men, the longer spermatogenesis period also raises the risk of chromosomal pairing and segregation mistakes. Additionally, research indicates that cellular checkpoints that guarantee proper chromosome segregation may become less effective with aging, allowing errors to continue. Lifestyle variables like smoking, alcohol consumption, and exposure to environmental contaminants can exacerbate these symptoms and increase the risk. While men are less often than women to experience nondisjunction, understanding paternal age-related characteristics is critical for genetic counselling and assessing the reproductive risks associated with advanced paternal age.

Epigenetic changes also play an important role in meiosis, affecting gene expression and chromatin structure. Changes in histones or DNA methylation can interfere with the expression of genes that control meiosis, which can impact chromosome pairing and segregation. Segregation faults, for instance, may result from changed methylation patterns in centromeric areas that impair the kinetochore's capacity to bind microtubules. Furthermore, age-related epigenetic alterations, such as loss of chromatin integrity, increase the likelihood of nondisjunction. Genetic and epigenetic factors work together to form a complex interplay that affects chromosomal stability, with implications for disorders such as Down syndrome, Turner syndrome, and miscarriages, highlighting their importance in genetic counselling and therapeutic research [18].

Environmental Factors: Environmental influences significantly increase the possibility of chromosomal non-disjunction by altering the cellular processes that insure the normal chromosome segregation during cell deviations. Pesticides, heavy metal and industrial contaminates have all been related to disturbances in meiotic machinery [19]. This compound has the potential to produce oxidative stress, which may result in spindle abnormalities, DNA damage and

chromosomal alinement problems. DNA double stand may be cause by ionizing and UV radiation, which raises the risk of chromosomal miss segregation if the damage is not completely repaired. Life style factors, including as smocking and alcohol consumption, increase this risks by producing reactive oxygen spices (ROS), which damage protein involved in cohesin and kinetochore function. Increased ROS can also effect the Spindle assembly checkpoint (SAC), which allows cells with mismatch chromosome to divide. Moreover, its known that several treatments and medications, such therapeutic agent alter microtubule dynamic which raises the chances of disjunction.

Consequences of Non-disjunction:

Aneuploidy: Aneuploidy is a disorder defined by an abnormal number of chromosomes, which can result in genetic imbalances with serious biological and clinical repercussions. It is caused by chromosome segregation mistakes known as nondisjunction, which can occur during either meiosis or mitosis. Infertility, developmental problems, and miscarriages are all largely caused by aneuploidy. Common forms include Down syndrome, Klinefelter syndrome, Edwards syndrome, and Turner syndrome [20]. A major risk factor is advanced maternal age because meiotic process efficiency and oocyte quality deteriorate with age. Genetic mutations that disrupt proteins involved in chromosomal cohesion or spindle assembly, as well as environmental factors such as oxidative stress, can all raise the risk. Aneuploidy alters gene dosage balance, resulting in aberrant development, organ malfunction, or decreased survivability. The advancement of genetic counselling, prenatal diagnostics, and therapeutic approaches to address related illnesses depend heavily on its investigation.

Down Syndrome: Down syndrome, often called trisomy 21, is a genetic disease caused by an extra copy of chromosome 21. The disorder is caused by a chromosomal non-disjunction event in gametogenesis, in which the chromosomes fail to split properly during meiosis I or II. As a result, each gamete has an extra copy of chromosome 21. During fertilization, this gamete combines with a regular gamete, resulting in a zygote that has three copies of chromosome 21 in all of its cells rather than the customary two. Several mechanisms, like as non-disjunction, translocation, or mosaicism, might cause this trisomy.

Meiotic non-disjunction is the most prevalent cause, accounting for around 95% of cases, and it is closely connected with advanced maternal age. The weakening of cohesins, spindle abnormalities, and faulty segregation of chromosome 21 can result from the protracted stoppage of oocytes in meiosis I over a period of decades. About 4% of cases result from Robertsonian translocation, in which a piece of chromosome 21 joins to another chromosome, usually chromosome 14. The extra genetic material from chromosome 21 interferes with normal development in these situations, even while the total number of chromosomes stays at 46. Mitotic nondisjunction during fertilization causes a mixture of normal and trisomic cells in the body, which causes mosaic Down syndrome, which affects approximately 1% of cases.

An additional copy of chromosome 21 causes a series of cellular and molecular problems. The overexpression of more than 200 genes on chromosome 21 affects several biological processes, resulting in the traits that define Down syndrome. DSCAM and DYRK1A are two important genes that have been implicated; both genes impact neuronal development and are linked to developmental delays and intellectual disability [21]. Increased reactive oxygen species (ROS) can harm cells and tissues when SOD1, a gene implicated in oxidative stress regulation, is overexpressed. The genetic imbalance is exacerbated when an extra copy of chromosome 21 interferes with the expression of genes on other chromosomes.

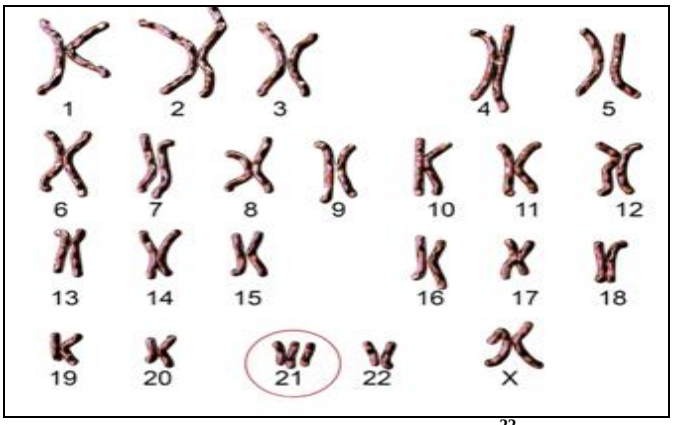

FIG. 4: DOWN SYNDROME [22]

Klinefelter Syndrome: Klinefelter syndrome is a genetic condition that's effects males who are bone with an extra X chromosome, resulting in the karyotype 47+XXY. It is the one of the most prevalent chromosomal disease effecting around one in every 500 to 1000 male births. Non-disjunction during meiosis in the maternal egg or paternal spermduring the initial mitotic division during fertilization, leads to the formation of the extra X chromosome. The excessive amount of genetic material interferes with normal development, resulting in a verity of physical neurological and reproductive characteristic. Depending on the degree of the chromosomal abnormalities the syndrome can also have variants like 48+XXXY or mosaicism, which can case milder or more severe syndrome [23].

Klinefelter syndrome is defined by testicular dysfunction, which results in deceased levelled of testosterone. During puberty the hormonal imbalance lead to delayed or incomplete sexual development. Gynecomastia, decreased facial and body hair and trine testis are common syndrome. Due to reused testosterone level many people also have tall height because the growth plates in their bones a longer to close infertility is a common result of Azoospermia, though other men may have limited sperm production and quality for assisted reproduction.

This syndrome characteristic by a wide range of psychological and behavioural characteristic. People may have learning challenges, especially in language and reading, and speech development delays, even though their intelligence is usually within the normal range. Executive functioning skills, such as planning, organization, and attention, may also be compromised [24]. Social and emotional problems, such as sadness and anxiety, are prevalent, and some people may struggle to build relationships with others or read social cues. Early detection and intervention can greatly improve outcomes in these areas.

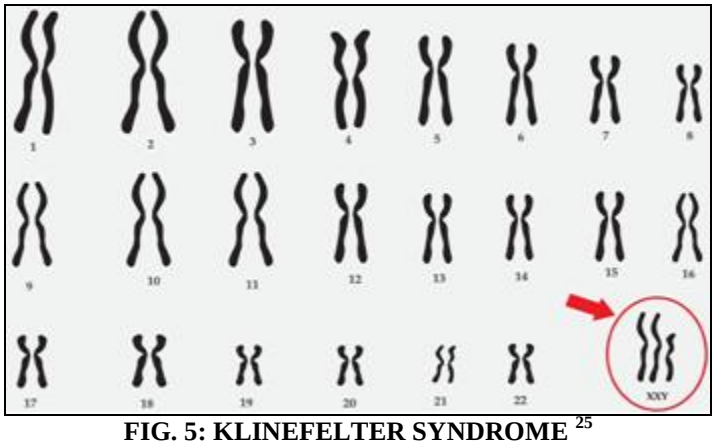

FIG. 5: KLINEFELTER SYNDROME [25]

Edwards Syndrome: Edwards syndrome, commonly known as Trisomy 18, is a serious chromosomal condition caused by an extra copy of chromosome 18 in an individual's cells. Non-disjunction is a random mistake in cell division that occurs during egg or sperm production. Many physical, developmental, and intellectual difficulties result from this extra chromosome's disruption of normal development. It is more prevalent in pregnancies that end in miscarriage or stillbirth, but Edwards syndrome is the second most common trisomy disorder after Down syndrome, occurring in about 1 in 5,000 live births. Babies born with Edwards syndrome have a particular set of clinical characteristics. Physical characteristics may include a small, improperly shaped skull (microcephaly), low-set ears, cleft lip or palate, a small jaw, and clinched hands with overlapping fingers [26]. Over 90% of new-borns with heart defects have one of the common heart defects, such as ventricular or atrial septal defects. Gastrointestinal abnormalities, renal deformities, and breathing difficulties are also common. Muscle underdevelopment increases physical weaknesses, and growth retardation, both prenatal and postnatal, contributes to a feeble look. These kids frequently have epilepsy, significant developmental delays, and severe intellectual disabilities. Individuals suffering with Edwards syndrome have a dismal prognosis. Of those born alive, most do not live

past the first year, and many afflicted pregnancies end in miscarriage or stillbirth. Around 10% of live-born babies make it to their first birthday, and a small percentage of them survive into adolescence or adulthood with close medical supervision [27]. The severity of organ abnormalities and the availability of comprehensive medical therapies have a significant impact on survival rates and quality of life.

Prenatal screening and diagnostic techniques are critical for the detection of Edwards syndrome. Increased nuchal translucency or structural abnormalities are examples of possible indicators of the disorder that can be found using non-invasive techniques including maternal serum screening and ultrasonography [28]. Confirmatory diagnostic techniques, such as amniocentesis or chorionic villus sampling, examine foetal cells for the presence of additional chromosome 18. Developments in genetic testing, like cell-free foetal DNA testing, have greatly increased the precision of early detection, empowering families to make well-informed choices on child care.

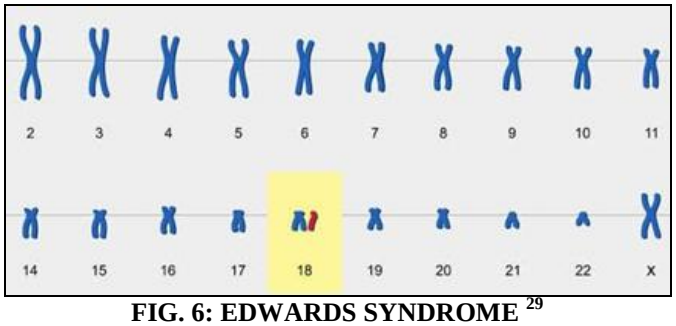

FIG. 6: EDWARDS SYNDROME [29]

Turner Syndrome: Turner syndrome (TS) is a female-specific chromosomal condition caused by the partial or total loss of one of the two X chromosomes. This issue affects around one in every 2,500 live female births, making it one of the most prevalent sex chromosomal abnormalities. Monosomy, mosaicism, and structural abnormalities such as a missing X chromosome are among the genetic disorders that can cause Turner syndrome. These variances result in a variety of physical and developmental characteristics, with severity and presentation varying widely across people.

Turner syndrome effects woman and girl differentially. When growth hormone therapy is felt to work, people with TS have and average adult height that is significantly smaller than the normal population. Physical characteristic include are webbed, a lower hair line at the base of the neck, a broth chest with widely separated nipples and lymphedema [30]. Children with TS are often born with heart defects such as coarctation of the aorta or bicuspid valve, which required regular monitoring and sometime surgery. Common side-effect of the disease includes thyroid problem, kidney problem and hearing loss.

Patient with turner syndrome are specially worried about they are reproductive health. The majority TS female have ovarian in sufficiency, that case by undeveloped or malfunctioning ovaries. While adult option for contraception may be provided via assisted reproductive technologies like egg donation, infertility and delayed or absent puberty and the typical outcome. Hormone replacement therapy is often use to maintain bone health and establish secondary sexual characterises because people who have TS are prone to develop osteoporosis.

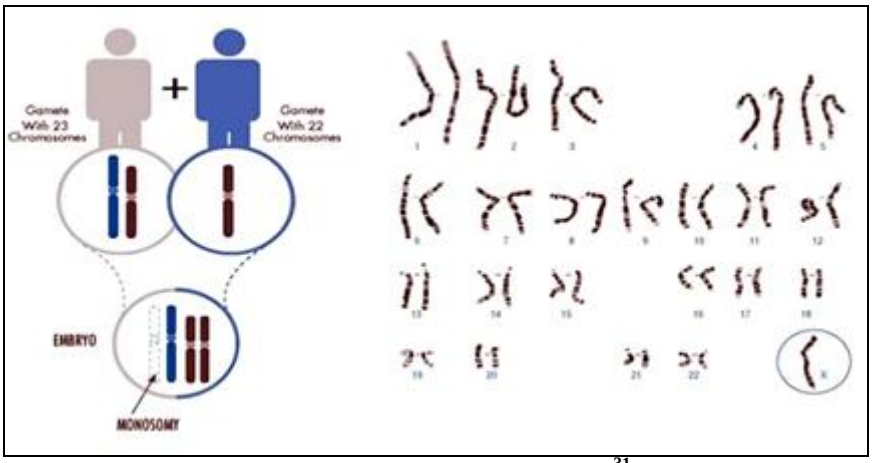

FIG. 7: TURNER SYNDROME [31]

Detection and Diagnosis:

Prenatal Testing for the Diagnosis of Chromosomal Non-disjunction:

Non-Invasive Prenatal Testing (NIPT): Non-Invasive Prenatal Testing (NIPT) is a revolutionary method for detecting chromosomal non-disjunction during pregnancy. It is a cutting age screening technology that detected chromosomal non disjunction in foetal and provides a shape and effective alternative to evasive diagnostic treatment. It analysis cell-free foetal DNA in the maternal circulation, which is normally collected simple blood draw after the 10^{th} week of pregnancy. NIPT is extremely sensitive and specific for common aneuploidies, including down syndrome, Edward syndrome [32]. It can also detect sex chromosomal abnormalities such as turner syndrome and Klinefelter syndrome. Pregnant woman who are at high risk for chromosomal abnormalities because of their advance maternal age or family history, NIPT to be a desirable option because it does not pose any risk to the foetal [33].

Ultra Sound Screening: Ultra sound screening is a common non-invasive tool to determine the risk of chromosomal non-disjunction in a feta. It frequently occurs in the first and second trimesters pregnancy and involved comprehensive imagine to identify the physical markers known as soft signs link with chromosomal abnormalities. Nuchal translucency measurement is an essential characteristic, that analysis excess fluid at the back of the foetal neck and can be linked with down syndrome or other aneuploidies [34]. Potential chromosomal problems can be indicated by other signs such as anomalies, aberrant limb length or the absence of nasal bone. Using ultra sound screening in conjunction with maternal blood testing for biochemical markers like hCG and PAPP-A improved the accuracy of risk assessment. Despite being unable to concussively diagnose non-disjunction, its provides useful information to identify pregnancy and higher risk,assisting in the selection of confirmatory test such as chronic villus collection or amniocentesis. Ultrasound screening is a vitalcomponent of prenatal treatment because of its accessibility and non-invasive nature [35].

Chorionic Villus Sampling: Chorionic villus sample (CVS) is an invasive prenatal diagnostic method that detected chromosomal non-disjunction and other genetic abnormalities. CVS is often performed between the 10^{th} and 13^{th} weeks of pregnancy, includes the collection of chorionic villus tissue form the placenta using a trans abdominal or trans cervical roots determine by ultra-sonography. Aneuploidies such as down syndrome, turner syndrome and sex chromosome abnormalities can be detected by analysing the cells in the chorionic villi using the technique like FISH or Microarray analysis as they possess the identical genome as the foetal. CVS enables and earlier diagnosis than amniocentesis providing parents more time to make decision, there is a small risk of complication such as bleeding, infection and miscarriage[36]. Pregnancies with high risk such as those with advance maternal age aberrant screening results or a family history of genetic diseases are usually advised to used CVS as a conclusive diagnostic test.

Postnatal Testing for Diagnosing Chromosomal Non-disjunction:

Karyotyping: Karyotyping is a basic cytogenetic technique that implores visual analysis of a cell's chromosome number and structure to determine chromosomal non-disjunction. Cells are culture, generally form amniotic fluid chorionic villi or peripheral blood, and then stopped in metaphase, when the chromosome are most visible. The chromosome is then dyed and place in a uniform pattern, enabling for the detection of aneuploids such as down syndrome, turner syndrome. Karyotyping can also detect structural abnormalities that may arise form defective chromosomal segregation such as duplication, deletions or translocations. Karyotyping is a essential part of genetic testing because it may offer a comprehensive chromosomal profile and detected non-disjunction event, despised being time consuming and requiring expert interpretation [37].

Fluorescence *In-situ* Hybridization: Fluorescence *In-situ* Hybridization (FISH) is a molecular cytogenic technique used to detected chromosomal non-junction and associated disorder with high specificity and speed. In ordered to visualise chromosomal number and structural alteration under a Fluorescence microscope, fluorescently tagged DNA probes are used, which attached to particular chromosome region. FISH is commonly use in both prenatal and postnatal setting to

diagnosis aneuploids such as Trisomy 21, Trisomy 18 and Klinefelter syndrome [38]. FISH is quicker than karyotyping and it is especially helpful for focused examination when a particular chromosomal issue is detected.

Array Comparative Genomic Hybridization: Chromosomal non-disjunction and other genomic abnormalities can be detected with high resolution using the sophisticated molecular approach known as Array Comparative Genomic Hybridization (aCGH). A micro arrayplatform is used to compare a patient's DNA to a reference DNA sample. The procedure involved identifying both DNA sample with various fluorescence dyes and hybridization them to a chip containing hundreds of genomic proved. Aneuploids such as Trisomy 21and more sever genomic imbalances like micro deletions or duplication can be detected by analysing variation in fluorescence intensity's across the array which signal changes in copy number, aCGH is quicker and more suited for detecting microscopic chromosomal alteration that might not be apparent under microscope because it does not require cell culture in comparison to standard karyotyping procedure [39].

Quantitative Polymerase Chain Reaction: Quantitative Polymerase Chain Reaction (qPCR) is an efficient asensitive molecular approach for detecting chromosomal non-disjunction by measuring DNA copy numbers. The technique entails increasing particular DNA areas that correspond to chromosome that are often involved in aneuploids. Losing fluorescence dyes the application processes is tracked in real time and the amount of DNA is correlated with the fluorescence intensity. qPCR can detect disease like Trisomy 21, and Monosomy X by comparing the relative abundance of these areas to the reference genes qPCR is a useful technique for diagnosing non-disjunction both during pregnancy and after delivery because of its great's sensitivity, rapidity and affordability [40]. In high throughput screening or urgent diagnosis situation its targeted approach is very useful in verifying individual aneuploids.

Whole-Genome Sequencing: Whole-Genome Sequencing (WGS) is a through and high-resolution approach for detecting chromosomal non-disjunction and other genetic disorder that examines, and individuals complete genomic sequence. WGS compared to target methods provide comprehensive information on the number and structure or chromosome, making it's possible to identify smaller copy number variations, structural rearrangement and even single nucleotide variants as well as aneuploids by sequencing billions of DNA fragments and compering them to a reference genome, WGS can discover the presided chromosomal areas impacted by non-disjunction [41].

Prevention and Management:

Genetic Counselling: Genetic counselling is an essential step in the prevention and treatment of chromosomal non-disjunction syndromes such Down syndrome, Turner syndrome, and Edwards syndrome. The hereditary foundation of these disorders, the likelihood of recurrence, and the available options for family planning and care are all explained to individuals and families. Counselling couples considering pregnancy involves determining risk factors such as advanced maternal age, a history of aneuploidy, or genetic testing to determine carrier status. Preimplantation genetic testing (PGT) during in vitro fertilization (IVF) can detect chromosomal abnormalities in embryos, hence reducing the risk of impacted pregnancies [42].

Genetic counsellors assist families in comprehending non-disjunction syndromes, their prognosis, and available treatments when they are identified either prenatally or postnatally. They also help families find resources for community support and medical care, as well as emotional support. Families that receive genetic counselling are better equipped to manage chromosomal problems and achieve better results.

Assisted Reproductive Technologies: Assisted reproductive technologies (ART) serve an important role in preventing and treating chromosomal non-disjunction disorders, providing hope to individuals and couples at risk. One essential method for screening embryos prior to implantation is the combination of IVF and preimplantation genetic testing (PGT). PGT detects aneuploid embryos and selects chromosomally normal ones for transfer, dramatically lowering the likelihood of Down syndrome, Edwards syndrome,

and Turner syndrome [43]. This strategy is especially helpful for older women, whose aging eggs increase their risk of non-disjunction. When genetic problems are found in one of the partners, ART also includes more sophisticated techniques like egg or sperm donation [44]. These technologies offer options for families with a history of chromosomal problems in addition to increasing the likelihood of a safe pregnancy. Families can ensure improved reproductive outcomes by making educated selections by combining ART with genetic counselling.

Public Health Interventions: Public health measures that emphasize education, early detection, and access to healthcare are essential in the prevention and management of chromosomal nondisjunction diseases. Awareness campaigns educate the public about risk factors such as advanced maternal age and the value of prenatal care, allowing them to make educated reproductive decisions [45]. Programs that promote routine prenatal screenings, such as non-invasive prenatal testing (NIPT) and maternal serum screening, aid in the early detection of chromosomal abnormalities such as Down syndrome and Turner syndrome.

CONCLUSION: Chromosomal non-disjunction is a crucial defect that occurs during meiosis and mitosis, when chromosomes fell to separate properly, resulting in an incorrect number of chromosomes in daughter cells. Non-disjunction can occur during the first and second meiotic division, with each contributing unique genetic effect. The impact of spindle assembles, chromated cohesion and age-related factors are emphasized by understanding of the mechanism of non-disjunction, specialin female gametogenesis where the risk rises with maternal age. The phenomenon emphasized the important aquert chromosomal segregation is to be maintaining organismal health and genomic integrity. The objective of genetic research advancement like molecular studies and prenatal diagnostic which to detect to reduce the effects of chromosomal non-disjunction.

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