



## AN OVERVIEW OF DOWN SYNDROME

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DOI: <https://doi.org/10.47957/ijciar.v7i2.174>

Received: 28 Apr 2024 Revised: 11 May 2024 Accepted: 05 June 2024

### Abstract

The most prevalent chromosomal disorder linked to intellectual disability is down syndrome, often known as Down's syndrome (DS), which is marked by a number of distinct clinical symptoms. About 1 in 800 newborns globally experience it. Approximately 500 live births are caused by DS each year in the US, while over 200,000 people are affected by the disorder. The first account of the syndrome dates back to 1866 and is credited to the English physician John Langdon Down of Cornwall. When the chromosomal cause of the disorder was identified more than 90 years later, it was termed Down syndrome. Although there is still inequality in access to health care and other supportive services, the potential for the development and socialization of people with Down syndrome has been more widely recognized, and early support for impacted children and their families is extensively adopted. Patients vary greatly in their phenotypic characteristics; intellectual disability is typically moderate but can be mild to severe, and social function is frequently good in comparison to cognitive impairment. Geographical location and ethnic origin also have an impact on the incidence and presentation of DS.

**Keywords:** Down syndrome, autosomal aneuploidy, mortality, phenotype: trisomy21.

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### Introduction

Down syndrome is a genetic disorder is caused by an extra copy of chromosome 21. This can happen in three different ways. In the majority of cases people with Down's syndrome have an extra copy of chromosome 21 in every cell in their body (trisomy 21). In 3-4% of cases, the extra chromosome attaches to another chromosome pair – this is called translocation. Mosaic Down's syndrome occurs in 1-2% of people with Down's syndrome and is where some of the cells in the body have an extra copy of chromosome 21 and some do not. Different physical features of a new-born baby with Down's syndrome are often detected by the Paediatricians who will order a blood test to investigate the genetic makeup of the child. This will confirm the Down's syndrome, and the families will be told what type of Down's syndrome their child has. kids with Down's syndrome are less resistant to infections and may need extra help to recover due to lowered immune systems. It is common for our young children to spend most of the winter fighting colds and viruses, and due to small airways may seem to constantly have a runny nose. Children with Down's syndrome may need extra time off school to recover from their illnesses. Children with Down's syndrome is 10 to 20-fold more likely to develop leukaemia. With appropriate treatment, many children with Down's syndrome and leukaemia can be successfully treated. Thyroid disorders are more common in children with Down's syndrome, and most will undergo regular testing of their thyroid levels. (1)

#### Types of down syndrome:

- Trisomy of chromosome 21:

Trisomy is the most common type of Down syndrome. It accounts for 95% of cases of Down syndrome. There is one extra chromosome 21. The total number of chromosome present is 47 instead of the normal 46 chromosomes. The main cause of trisomy is Nondisjunction of chromosome 21 during meiosis at the time of gamete formation. The irregular cell with trisomy of chromosome 21 is fertilised giving rise to trisomy in all the cells of the foetus.

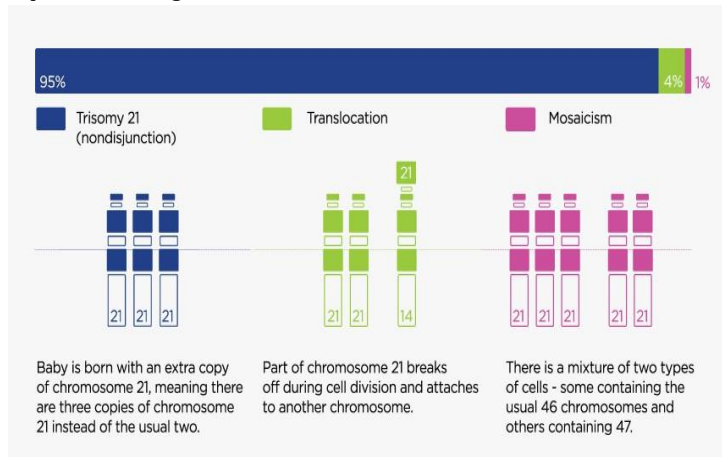
- Mosaicism:

This is the rare form of Down syndrome, accounting for only 1% of the total cases.

In this type of Down syndrome, some cells are normal having 46 chromosomes and some cells have abnormal 47 chromosomes. Symptoms may be less prominent in mosaicism. Mosaicism is caused when nondisjunction occurs during mitotic division in the zygote after fertilization. It results in some normal cells and some cells with trisomy of 21. (2)

**Translocation down Syndrome:**

This type of Down syndrome accounts for 4% of the total cases. Here an extra chromosome 21 is not present but there is an extra part of the chromosome 21 present attached to a different chromosome. Total 46 chromosomes are present of which one is abnormal. This is due to the translocation of the long arm (q arm) of chromosome 21 to another chromosome during the replication process. The extra portion often gets translocated to chromosome 14.



**Fig 1 types of Down syndrome**

**Characteristics:**

1. Short stature.
2. Poor muscle tone.
3. Small nose with flat bridge.
4. Short neck.
5. Small head and flat face.
6. Broad hands and feet.
7. Poor balance.
8. Poor vision and audition.
9. Delays or deficits.
10. Slowness of movement.
11. Small low-set ear.

**Symptoms of Down syndrome:**

- Short stature and stunted growth.
- Fold of the skin above the eye, slanted nose.
- Mental retardation.
- Cardiac deformities.
- Single transverse palm crease and is broad and short.
- Poor muscle tone and excessive flexibility.
- Small head, short neck and abnormal teeth.



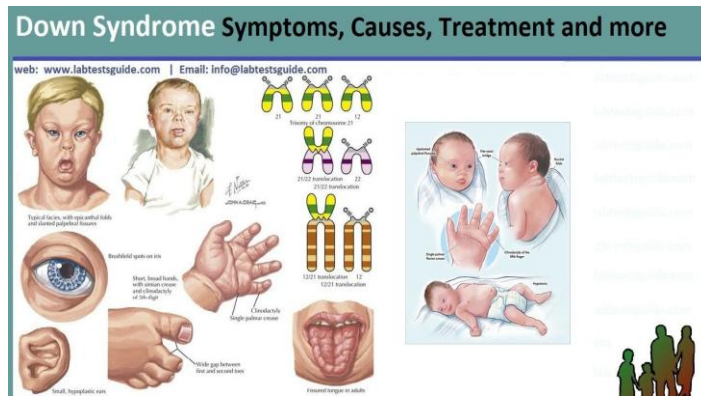
**Fig 2 symptoms of down syndrome**

**Etiology:**

Etiology Genes of the extra chromosome 21 are responsible for all of the Characteristics of Down syndrome in most cases [US National Library of medicine, 2008]. However, in a recent; it has been noted that who have had a baby with down syndrome had hand abnormality in how their body's metabolism the B vitamin folic acid. If this can become pregnant to take daily multivitamin containing 400 micrograms of folic acid which has been shown to reduce risk of brain and spinal cord defects (children's hospital of the king's daughters, 2007).(3)

**Causes**

DS is caused by an extra copy of chromosome number 21 inside each of the body's cells. It is a chromosomal accident, not caused by anything the parents have done before or during the pregnancy, and is only very rarely inherited. Our bodies are made up of billions of cells. Within each cell lie the fundamental units of inheritance, known as genes. These are bundled into packages called chromosomes, which can be seen under the microscope. (4)



**Fig 3 symptoms, causes, treatment**

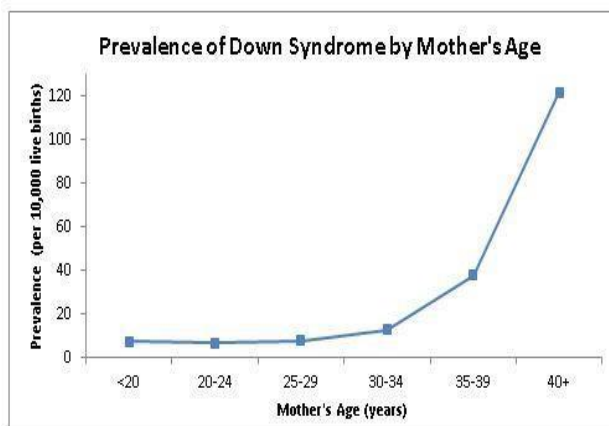
**Epidemiology:**

According to World Health Organization; the predictable incidence of DS is between 1 in 1,000 to 1 in 1,100 live births all over the world. The difference in prevalence among populations or countries or in the same population over time will depend on the potential risk factors in common for that community.

**Complications:**

Approximately half the children with Down syndrome are born with some type of heart defect. These heart problems can be life-threatening and may require surgery in early infancy. • Leukemias. Young children with Down syndrome are more likely to develop leukemias than are other children. (5)

Infectious diseases. Because of abnormalities in their immune systems, those with Down syndrome are much more susceptible to infectious diseases, such as pn Heart defects. Approximately half the children with Down syndrome are born with some type of heart defect. These heart problems can be life-threatening and may require surgery in early infancy. leukemias. Young children with Down syndrome are more likely to develop leukemias than are other children. Infectious diseases. Because of abnormalities in their immune systems, those with Down syndrome are much more susceptible to infectious diseases, such as pneumonia.



Dementia. Later in life, people with Down syndrome have a greatly increased risk of dementia. Signs and symptoms of dementia often appear before age 40 in people with Down syndrome.

Sleep apnea. Because of soft tissue and skeletal alterations that lead to the obstruction of their airways, children with Down syndrome are at greater risk of obstructive sleep apnea. Obesity. People with Down syndrome have a greater tendency to be obese

than does the general population Other problems.

Down syndrome may also be associated with other health conditions, including gastrointestinal blockage, thyroid problems, hearing loss, skeletal problems and poor vision.

Life expectancy Life spans have increased dramatically for people with Down syndrome. In 1929, a baby born with Down syndrome often didn't live to age 10. Today, someone with Down syndrome can expect to 50 and beyond, depending on the severity of his or her health problems. Life span continues to increase because of early interventions and better eunoia. Dementia. Later in life, people with Down syndrome have a greatly increased risk of dementia. Signs symptoms of dementia often appear before age 40 in people with Down syndrome. Sleep apnea. Because of soft tissue and skeletal alterations that lead to the obstruction of their airways, children with Down syndrome are at greater risk of obstructive sleep apnea.(6)

Obesity. People with Down syndrome have a greater tendency to be obese than does the general population other problems. Down syndrome may also be associated with other health conditions, including gastrointestinal blockage, thyroid problems, hearing loss, skeletal problems and poor vision.

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Heart defects. Approximately half the children with Down syndrome are born with some type of heart defect. These heart problems can be life-threatening and may require surgery in early infancy. • leukemias. Young children with Down syndrome are more likely to develop leukemias than are other children. (7)

**Risk Factors:**

The only known non-genetic risk factor for having a child with Down syndrome is what is sometimes referred to as advanced maternal age (being over 35). This doesn't mean, however, that having a baby before age 35 is a reliable strategy for preventing Down syndrome. Roughly 80% of children with Down syndrome are born to women who are younger than 35. Here is how the risk of Down syndrome increases with maternal. Some parents have a greater risk of having a baby with Down syndrome.

- Risk factors include:

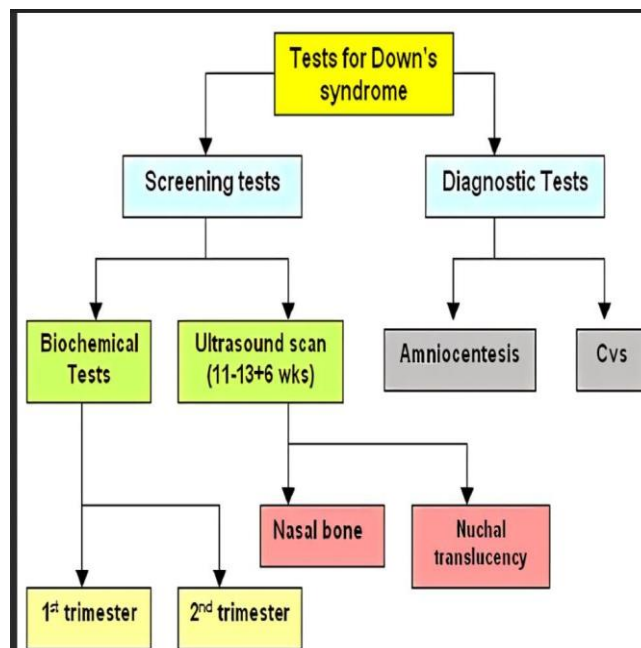
maternal age. A woman's chances of giving birth to a child with Down syndrome increase with age because older eggs have a greater risk of improper chromosome division. A woman's risk of conceiving a child with Down syndrome increases after 35 years of age. However, most children with Down syndrome are born to women under age 35 because younger women have far more babies.

Being carriers of the genetic translocation for Down syndrome. Both men and women can pass the genetic translocation for Down syndrome on to their children. (8)

Having had one child with Down syndrome. Parents who have one child with Down syndrome and parents who have a translocation themselves are at an increased risk of having another child with Down syndrome. A genetic counsellor can help parents assess the risk of having a second child with Down syndrome.

Age	Risk
25	1 in 1,250
30	1 in 900
35	1 in 350
40	1 in 100
45	1 in 30
49	1 in 10

Fig 5

**Diagnosis of down syndrome:**

Prevention of DS depends upon offering prenatal diagnosis to high-risk pregnancies via amniocentesis and chorionic villus sampling (CVS). Amniocentesis and CVS are quite reliable but offers risk of miscarriage of between 0.5 to 1%. Based soft markers like small or no nasal bone, large ventricles and nuchal fold thickness, the risk of DS for fetus can be identified through ultrasound generally at 14 to 24 weeks of gestation. Increased fetal nuchal translucency indicates an increased risk of DS. The other methods used for prenatal diagnosis in which traditional cytogenetic analysis is still widely used in different countries. However, some rapid molecular assays FISH (fluorescent in situ hybridization), QF-PCR (quantitative fluorescence PCR), and MLPA (multiplex probe ligation assay)- also used for prenatal diagnosis. (9)

**Routine karyotyping Cytogenetic:**

Analysis of metaphase karyotype remains the standard practice to identify not only trisomy 21, but also all other aneuploidies and balanced translocations. Details on diagnostic methods with advantages and disadvantages are mentioned in Table 2. Rapid aneuploidy testing methods Over the past 10 years however, several other methods have been developed and used for the rapid detection of trisomy 21, either in fetal life or after birth. The most widely used is FISH of interphase nuclei, using Has 21- specific probes or whole-Has 21. An alternative method that is now widely used in some countries is QFPCR, in which DNA polymorphic markers (microsatellites) on Has 21 are used to determine the presence of three different alleles. This method relies on informative markers and the availability of DNA. Rapid diagnosis by PCR-based methods using polymorphic STR markers may reduce these difficulties using conventional approach. Using STR markers method we can detect trisomy in 86.67% cases with only two markers. Using a greater number of markers can further increase the reliability of the test. Simultaneously parental origin of the nondisjunction can also be detected. It is based on hybridization and PCR method and is divided into four steps: DNA denaturation, hybridization of probe to the complementary target sequence, probe ligation and PCR amplification. And finally capillary electrophoresis of PCR amplified products is carried out. However, MLPA is unable to exclude low level placental and true mosaicism. (10)

**Advancement in the diagnosis:**

A recent method, termed paralogous sequence quantification (PSQ), uses paralogous sequences to quantify the Has 21 copy number. PSQ is a PCR based method for the detection of targeted chromosome number abnormalities termed paralogous sequence quantification (PSQ), based on the use of paralogous genes. Paralogous sequences have a high degree of sequence identity, but accumulate nucleotide substitutions in a locus specific manner. These sequence differences, which are termed as paralogous sequence mismatches (PSMs), can be quantified using pyrosequencing technology, to estimate the relative dosage between different chromosomes.

PSQ is a robust, easy to interpret, and easy to set up method for the diagnosis of common aneuploidies, and can be performed in less than 48 h, representing a competitive alternative for widespread use in diagnostic laboratories. The sequencing is quantitatively done by using pyrosequencing. Finally, comparative genomic hybridization (CGH) on BAC chips can be used for the diagnosis of full trisomy or monosomy, and for partial (segmental) aneuploidies.

**Non-invasive Prenatal diagnosis:**

Fetal cells in maternal circulation: Ever since the discovery of presence of fetal lymphocytes in maternal blood was made in 1969, the investigators are trying to develop genetics-based non-invasive prenatal diagnostics (NIPD). Despite several advantages offered by this approach, the use of fetal cells for NIPD has never reached clinical implementation because of their paucity (on the order of a few cells per milliliter of maternal blood) and concerns of fetal cell persistence in the maternal circulation between pregnancies.

Cell free fetal DNA from maternal serum: This novel approach was proposed in 1997. Cell-free fetal DNA constitutes between 5% and 10% of the total DNA in maternal plasma and increases during gestation and rapidly clears from the circulation post-delivery. Several clinical applications based on the analysis of cell-free fetal DNA have been developed like determining fetal.

**Treatment of down syndrome:**

There is no single, standard treatment for Down syndrome. Treatments are based on each individual's physical and intellectual needs as well as his or her personal strengths and limitations.<sup>1</sup> People with Down syndrome can receive proper care while living at home and in the community. A child with Down syndrome likely will receive care from a team of health professionals, including, but not limited to, physicians, special educators, speech therapists, with children with Down syndrome should provide stimulation and encouragement. (11)

Children, teens, and adults with Down syndrome also need the same regular medical care as those without the condition, from well-baby visits and routine vaccinations as infants to reproductive counseling and cardiovascular care later in life. Like other people, they also benefit from regular physical activity and social activities. Early Intervention and educational therapy.

- Treatment Therapies.
- Drugs and Supplements.
- Assistive Devices.

A clinical trial of the drug in people with the disorder is currently underway. Small studies of a second Alzheimer’s drug, donepezil (Aricept), have shown mixed results in people with Down syndrome. Early Intervention and Educational Therapy. Treatment Therapies, Drugs and Supplements Assistive Devices. (12)

**Standard treatment guideline for down syndrome:**



Treatment is directed at addressing the individual concerns of a particular individual (e.g. Certain heart defects may require surgery). Timely surgeries for cardiac and GI anomalies are necessary to prevent serious complications. Because the risk of vision problems, hearing loss, and infection is increased, screening and treatment may be necessary. Nursing Management: Nurses should obtain a history of mother’s pregnancy, birth history, & genetic testing. Observe physical characteristics of DS. (13)

Assess the following: Respiratory functioning due to poor muscle tone Heart sounds for presence of a murmur Infant’s ability to eat due to protruding tongue & mouth breathing Bowel functioning In an older child, assess height & weight and compare to appropriate growth chart Cognitive development Skin integrity due to tendency toward dry, rough, cracking skin Determine family knowledge, coping, & support Observe interaction & bonding between mother & infant Parental feelings about having a child with Down Syndrome.

### **Prevention & Education:**

- 1) No prevention for DS
- 2) Absolutely nothing that anyone can do to prevent a trisomy & there is nothing that anyone can do to cause a trisomy.
- 3) Efforts of prevention are aimed at genetic counselling of couples who are preparing to have babies.
- 4) Screening test of AFP to determine chances.
- 5) Teach parents the importance of food & fluids to maintain adequate nutrition.
- 6) Emphasize the need to balance adequate nutrition. Poor feeding can result in obesity later in life.
- 7) Teach family how to prevent physical complications.
- 8) Avoid infection by engaging in good hand washing.
- 9) Increase fibre in diet to avoid constipation Encourage physical activity.
- 10) Advise parents to seek regular check-for their child unit.

### **Conclusion and Future Directions**

At this point, it is not advised for parents to provide EGCG to their affected children. It makes sense, though, that nervous parents would find this difficult as they would have to wait for the results of longer-term clinical trials and would not have been able to intervene for their affected children early on. Undoubtedly, the discussion around Down syndrome will go on for a while. Down syndrome cannot be prevented. You might wish to speak with a genetic counselor before getting pregnant if you have a high chance of having a child with Down syndrome or if you already have one. Understanding your odds of having a child with Down syndrome might be aided by consulting with a genetic counsellor. Along with discussing the benefits and drawbacks of testing, he or she can also describe the many prenatal tests that are available. Trisomy 21, also known as DS, is the most prevalent chromosomal anomaly in live births and is linked to several congenital abnormalities. A number of theories have been proposed to improve our knowledge of the relationship between genotype and phenotype. A "critical region" located inside 21q22 was thought to be the cause of multiple Down syndrome symptoms, such as mental retardation, clinodactyly of the fifth finger, congenital heart malformations of the endocardial cushions, and craniofacial abnormalities, among other characteristics. Uncovering the common genes—APP, BACE2, PICALM, APOE, GATA 1, JAK 2, CRELD 1, and DSCAM—involved in DS-associated abnormalities is the main objective of this review. Additionally, a thorough explanation of how approaches are applied to prenatal diagnosis in DS is provided in this study. Midway through the 1990s, FISH—which allows for testing on uncultured amniocytes—was developed as a rapid method for determining aneuploidy. Rapid aneuploidy testing has expanded to include MLPA and QF-PCR in the last few years. NGS is one of the alternative techniques for screening cell-free fetal DNA using maternal plasma. Other than FISH, MLPA, and QF-PCR, these methods are not commercially available for the diagnosis of aneuploidy because of their high operating costs, labor-intensive protocols, and intricate data analysis. The treatment of these patients needs to be planned because DS is linked to a number of clinical problems.

### **Author contributions**

All authors are contributed equally.

### **Financial support**

None

### **Declaration of Competing Interest**

The authors have no conflicts of interest to declare.

### **Acknowledgements**

None

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