In Syndrome

Down Syndrome / Trisomy 21

Definition :

It is a genetic disorder caused by the presence of all or a portion of a third chromosome 21.

History :

- It was named after John Langdon Down who reported its clinical description in 1866.
- The suspected association of Down syndrome with a chromosomal abnormality was confirmed by Lejeune et al. in 1959.

Prevalance : 1 in 500.

Etiology :

On genetic basis :-

- Meiotic non dysjunction (95%) - Most common cause, it takes place at meiosis I and the extra copy of chromosome is from maternal origin.
- It has also been recorded that young age mothers (18 to 29 years) born to their mothers at the age 30 years and above produced as high as 91.3% of children with Down syndrome.
- The likelihood that a woman under 25 and 30 years who becomes pregnant will have a baby with Down syndrome is less than 1 in 1,400 and 1,000 respectively.
- Chance of having a baby with Down syndrome increases to 1 in 350 for women who become pregnant at age 35 and continues to increase as the woman ages, so that by age 42, and by age 49, the chance is 1 in 60 and 1 in 12 respectively.
- On the contrary there are reports that 80% of Down syndrome babies are born to young women of age less than 30 years.
- Robertsonian translocation (4%) - Translocation occurs before fertilisation. 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.
- The extra portion often gets translocated to chromosome 14(t14:21). So a person with translocation Down syndrome contains one chromosome 14, one chromosome 14/21 and a pair of normal chromosome 21.

- Mosaicism (1%) - The least common pattern of transmission and the error in cell division occurs after fertilisation.
- Affected individuals have some cells with an extra chromosome 21 and others with the normal number, and this results in some body cells containing 47 chromosomes and others having the usual 46 chromosomes.

Clinical features :

C – Congenital heart defects (AV septal defect, Endocardial cushion defect)
H – Hypotonia
I – Sandal gap
L – Leukemia
D – Duodenal atresia
H – Hirschsprung disease
A – Alzheimer's disease
S – Simian crease
P – Protruding tongue
R – Rolling of eyes
O – Flat occiput
B – Brushfield spots at Iris
L – Low nasal bridge
E – Epicanthal folds
M – Mongolian slant

Investigations :

- Prenatal chorionic villus sampling and/or amniocentesis with karyotyping.
- Amniocentesis and CVS are quite reliable but offers risk of miscarriage of between 0.5 to 1%.
- Postnatal karyotyping (if prenatal karyotyping not done).
- Diagnosis of Down syndrome may be suspected prenatally based on physical anomalies detected by
- Fetal ultrasonography
- Maternal serum screening
- Noninvasive prenatal screening (NIPT)
- Dual markers = hCG - $^{\downarrow}$, PAP-A - $^{\uparrow}$.
- Quadruple markers = hCG - $^{\uparrow}$, αFP - $^{\downarrow}$, Unconjugated Estriol - $^{\downarrow}$, Inhibin A - $^{\uparrow}$.

Prenatal USG Diagnosis :
Esophageal atresia, duodenal atresia - classic double-bubble sign, exomphalos, AVSD & VSD. Soft markers include ventriculomegaly, aberrant right subclavian artery, renal pelvic dilatation, echogenic intracardiac focus, short humerus & femur, increased nuchal fold thickness and hypoplastic nasal bone.

Treatment :

- The management of patients with Down syndrome is multidisciplinary.
- Treatment is basically symptomatic and complete recovery is not possible.

Recurrence risk :

- This is empirically estimated at 1%.
- If it's due to a parental balanced translocation, then the recurrence risk reaches 25%, since it becomes an autosomal recessive condition.

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