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Review Article

Types, Symptoms and Complications of Down syndrome

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Abstract

Background: Down syndrome (DS) is by far the most common chromosomal anomaly. It is caused by the involvement of one or half of the third copy of chromosome 21. An extra copy of chromosome 21 that can be either complete or partial based on the type, causes deformity and related morphological and physiological abnormalities in the body systems. Many people with DS have learning and memory disabilities, craniofacial defects and muscle hypotonia, and some have congenital heart. In addition, the magnitude of the defect is unpredictable. For instance, the degree of cognitive dysfunction varies considerably between individuals with DS.

Aim: In this review, we will look into types, symptoms and complications of Down syndrome.

Conclusion: Down syndrome is the most common chromosomal abnormality in live born infants associated with many congenital malformations. Many organs are involved in this syndrome so, ophthalmologist, orthopedic surgeon, cardiologist, dermatologist, gastroenterologist, physical therapist, mental health nurse, ENT surgeon and a behavior specialist should check up the child right after delivery. Parental education regarding management of Down syndrome is important, as parents need to be aware of the different possible complications associated with it for proper treatment.

Keywords: *Down Syndrome; Types of Down Syndrome; Complications of DS*

Introduction

Down syndrome (DS) is by far the most common chromosomal anomaly. It is caused by the involvement of one or half of the third copy of chromosome 21. An extra copy of chromosome 21 that can be either complete or partial based on the type, causes deformity and related morphological and physiological abnormalities in the body systems [1]. DS is now the most known congenital aneuploidy leading to delayed cognitive and physiological development [2]. Latest WHO figures of occurrence for DS varies from approximately to 11 in 10,000 live births worldwide. The incident rate is highest in mothers > 35 years of age and rises with more improvements in maternal health [3]. The incidence of DS is subjective to mother age and varies in different populations between 1 in 319 and 1 in 1000 live births [4]. National Down Syndrome Society report US population estimates 400,000 and 340,000 of persons with Down syndrome based on estimated birth prevalence [5].

Down's syndrome causes mental retardation and heart defects. In addition to a distinctive range of facial and physical symptoms, DS is consistent with congenital digestive tract abnormalities, elevated risk of cancers, immune response deficiencies, and Alzheimer's or dementia [6]. Many people with DS have learning and memory disabilities, craniofacial defects and muscle hypotonia and some have congenital heart. In addition, the magnitude of the defect is unpredictable. For instance, the degree of cognitive dysfunction varies considerably between individuals with DS [7]. People with DS experience a high rate of complications attributable to immunological and non-immunological causes. Inadequate antibody reactions and weak cell chemotaxis are among immunological causes [8].

Mongolism, Down's syndrome anomaly, Mongolian idiocy, Mongolian Idiots, Mongolian Imbecile, Mongoloid, Langdon Down anomaly, congenital acromicria or trisomy 21 anomaly are all expressions used to describe DS [9].

Low birth weight and poor growth velocity especially during the initial years are the first symptoms appear in children with Down syndrome [10]. DS also causes of fetal death (50% of fetal loss during pregnancy especially before 15 weeks of gestation). Many DS children receive additional education, while others may benefit from inclusive school settings [11]. Routine development testing in early years and then regularly during childhood will be beneficial in early detection of diet and overweight in these children [12].

While the evaluation of Down syndrome is primarily clinical, the golden standard is the chromosomal examination that reveals an additional copy of chromosome 21. Ultrasound during gestation between 14 and 24 weeks can be used as a screening tool as elevated nuchal fold length, minimal to no nasal bone and large ventricles are primary indications [13].

The care for patients with Down syndrome is an inter-professional initiative. Infants suspected of Down syndrome may have karyotyping performed to validate their assessment. Referral to the clinical geneticist for the genetic examination should be done and advice of both parents as well [14]. Education level of parents is one of the most critical facets of Down syndrome care, since caregivers need to be mindful of the many potential problems involved with Down syndrome, so that they'll be better diagnosed and managed. Treatment is primarily symptomatic and full rehabilitation is not possible [15]. A healthy diet, daily physical activity therapy is required for optimal development and excess weight, although the issues of eating do increase after heart surgery [16]. Latest developments in medical care and social integration have substantially improved the life span of people with DS [17].

In this review, we will look into types, symptoms and complications of Down syndrome.

Participants and Methods

Study design: Review article.

Study duration: Data were collected between 1 June and 30 October 2020.

Data collection Medline and PubMed public database searches have been carried out for papers written all over the world on the types and symptoms of Down syndrome. The keyword search headings included "down syndrome, types of Down Syndrome, complications of DS" and a combination of these were used. For additional supporting data, the sources list of each research was searched. Criteria of inclusion: the papers have been chosen on the basis of the project importance, including one of the following topics: down syndrome, types of Down Syndrome, complications of DS. Criteria for exclusion: all other publications that did not have their main purpose in any of these areas or multiple studies and reviews were excluded.

Statistical analysis

No predictive analytics technology has been used. In order to evaluate the initial results and the methods of conducting the surgical procedure, the group members reviewed the data. The validity and minimization of error were double revised for each member's results.

Types and genetics of Down syndrome

People with DS have a portion of chromosome 21 in some or all of their cells regardless the genetic variation between them. Duplication of a specific region of chromosome 21 can be responsible for DS main features [18]. Cytogenetic analysis and examination of all persons susceptible to DS is important to introduction a precise diagnosis and is obligatory in defining the recurrence risk of the syndrome in future generations [19]:

- **Trisomy 21:** This is the most frequent form of DS and the actual cause is unknown [20]. Trisomy 21 affects about 95% of all cases. It frequently occurs as a transient occurrence and recurrences are rare [18]. As recurrence happens, the theories are: gonadal mosaicism, parental predisposition to non-disjunction, the influence of hereditary causes and environmental exposure, as well as luck [21]. Trisomy 21 is used synonymously as DS, and the number 21 implies that it occurs at chromosome number 21 [22].

- **Mosaicism:** 1 per cent - 2 per cent of individuals with DS and an error in cell division happens after fertilization [23]. 2 distinct mechanisms for the development of mosaicism have been defined: one is a mitotic error in a regular, euploid zygote resulting in a mosaic embryo having 46/47, +21 karyotype, 45, -21 cell line being non-viable, while the other is a non-disjunction in familial gametogenesis followed by early postzygotic malsegregation of chromosome 21 [24,25]. A large percentage of mosaic families are born as trisomics. Like trisomy 21, the DS form of mosaic is not hereditary [26].

- **Translocation:** It is either Reciprocal, Robertsonian. Roughly 4 percent of people with DS have been translocated [27]. It happens prior fertilization as part of an extra copy of chromosome 21 disintegrates throughout cell division and is translocated to another chromosome in the egg or sperm cell [28]. Robertsonian translocations bear reproductive threats that rely on the genes involved and the sex of the family carrier. Reciprocal translocations are the most frequent type and require an interchange of chromosomes between each of the various forms, such as chromosome 1 and chromosome [29]. DS due to translocation is the only form that exists regardless of mother age and can be inherited by either parent. If no parent bears a Robertsonian translocation, the probability of recurrence of DS is minimal, close to that of free trisomy 21. People affected have 2 normal copies of chromosome 21 in addition to the extra chromosome 21 added [26].

Symptoms and complications

Various retained characteristics present in all DS populations, including intellectual disorders, craniofacial anomalies and early childhood hypotonia. People have a number of physical characteristics such as short chin, slanted brow, low muscle mass, smooth nasal bridge, palm crease and protrusion due to small mouth and large tongue. Other characteristics include large toe, abnormal fingerprint pattern, and small fingers [30,31]. Patients have a wide range of symptoms like intellectual and growing retardation or neurological defects, congenital heart defects, gastrointestinal (GI) abnormalities, characteristic facial features, and abnormalities [32]. Children with Down syndrome may also have other health issues that may hinder their growth. The occurrence of these conditions involves special treatment and medical help [12].

Learning, development and memory: All persons with DS experience some sort of memory and learning disability that differs in degree. And all people with Down syndrome have mild to severe intellectual difficulties [32]. Ranging levels of developmental disability and hypotonia are a constant characteristic of all Down syndrome patients as well as bad grades of motor, adaptive, eating, toilet sleep training and social learning at all ages relative to normal children. The most have an intelligence quotient (IQ) in a mild (50 -70) to moderate scale [33,34].

Neurologic defects: DS is distinguished by the early development of AD neuropathological characteristics and the subsequent onset of dementia. About 100 per cent of people with Down syndrome establish neuropathological characteristics of Alzheimer's disease by 40

years of age [35]. The risk of having early-onset Alzheimer's disease is considerably greater in people with DS with 50 to 70 per cent of dementia patients aged 60 years or older. About 7 percent of patients with DS can have autism as early as 2 or 3 years of age [36]. About 50 and 70 percent of individuals with DS experience dementia by the age of 60. The total incidence of epilepsy in Down syndrome is 1 - 13 percent with child spasms (IS) or West Syndrome (WS) being more frequent than the general population and requiring standard care [37]. Children with DS are also vulnerable to childhood spasms, but little is understood about the fundamental molecular mechanisms [38]. Individuals with DS have also been documented to have had disrupted sleep patterns. Lennox-Gestaut syndrome is also shown to be more common in children with Down syndrome as it occurs, has a delayed onset, and is correlated with reflex seizures, along with an elevated rate of EEG anomalies [39].

Cardiovascular defects: Heart defects are now the most frequent and contributing cause of mortality and morbidity in children with Down syndrome, particularly during the first 2 years of life. Involvement of heart defects is a critical aspect in longevity [40]. The prevalence of CHD in children born with Down syndrome is up to 50%. Another very prominent cardiac condition associated with Down syndrome is an atrioventricular septal defect (AVSD) that accounts for up to 40% of the cardiovascular disease defect in Down syndrome [41]. Endocardial cushion defect, also known as atrioventricular cushion defect, is by far the most frequent source affecting up to 40% of patients. Ventricular septal defect (VSD) is also found in this population, which affects up to 35% of patients [42]. Multiple morphological characteristics comprise muscular and membranous atrioventricular septum problems and the ovoid form of the typical atrioventricular conjunction. However, the surgical intervention and preservation of a child's nutritional condition remains the foundation before and after heart surgery [43]. Such cardiac abnormalities associated with trisomy 21 are secondary atrial defect (10 per cent), tetralogy of Fallot (6 per cent) and discrete PDA (4 per cent), whereas about 30 per cent of patients have more than one cardiac defect [44]. There is a regional difference in the occurrence of Down syndrome cardiac defect, with VSD being the most prevalent in Asia and ASD secondary in Latin America. The explanation for this disparity in the prevalence of different forms of CHD in different regions is still unknown and a variety of factors such as geographic similarity, have been established as contributing factors [45].

Gastrointestinal tract defects: Defects may appear everywhere from mouth to anus, although such abnormalities such as duodenal and small intestinal atresia or stenosis, annular pancreas, and imperforated anus have been reported to happen more frequently in these cases than in the general community [46]. Chronic constipation, stomach pain, frequent diarrhea and digestive problems are typical in these children. Celiac disease (CD) is seen in about 5 - 12% children with Down syndrome. GI defects like duodenal atresia (10%), Hirschsprung disease (1 - 3%), gastroesophageal reflux (1 - 4%), chronic constipation, diarrhea and celiac disease [47]. Surgical intervention with gastrointestinal abnormalities, GERD anti-reflux regimen, CD-free gluten and chronic constipation steps not attributable to Hirschsprung disease remain the same as with the public [48].

Cancer and leukemia: People with DS have a unique variety of cancers, including leukemia and solid tumors. Compared to the non-DS community people with DS have an increased risk of contracting leukemia [49]. The incidence of iron deficiency anemia is raised and the risk of acute leukemia is raised. Previous research suggests that DS patients have elevated relative risk of leukemia 10 - 20 times, with a median risk of leukemia at age 5 as 2% and 2.7% by age 30 [12]. Around 1 in 100 children with Down syndrome are at risk for developing acute lymphocytic and acute non-lymphocytic leukaemia. About 10% of patients with chronic myeloid leukemia (TML) experience acute megakaryoblastic leukemia (AMKL) leukogenesis by age 4 [50]. On the other hand; Yang et al., 2002 reported that individuals with DS are at lower risk of developing almost all types of malignant solid tumors indicating that trisomy 21 protects from tumor growth [33].

Endocrinal defects: Thyroid gland dysfunction is most commonly associated with Down syndrome. Hypothyroidism can be congenital or acquired at any time during life [51]. About half of the patients with Down syndrome Hyperthyroidism is much less frequent in patients with Down syndrome as compared to hypothyroidism, although the rate of it still exceeds the incidence of hyperthyroidism in the general pediatric population. Twenty to forty percent of children with DS can have thyroid abnormalities such as congenital hypothyroidism (1.8 - 3.6%), autoimmune thyroiditis (0.3 - 1.4%), Graves disease (2.5%) and compensated hypothyroidism (25.3 - 32.9%) [22,52].

Other defects: Children with Down syndrome are at an increased risk of reduced muscle mass because of hypotonia increased ligamentous laxity which causes retardation of gross motor skills and can result in joint dislocation [53]. Ear, nose and throat problems are also quite common in patients with Down syndrome. Hearing loss can be conductive or sensorineural and is seen in about 75% of children with DS [54]. Ophthalmological problems such as refractive errors (50%), strabismus (20 - 47%), cataracts (15%), nystagmus (10%), nasolacrimal duct obstruction, blepharitis (30%), keratoconus, defect in accommodation and retinal anomalies are quite common in children with Down syndrome [55].

Conclusion

Down syndrome is the most common chromosomal abnormality in live born infants associated with many congenital malformations. Many organs are involved in this syndrome so, ophthalmologist, orthopedic surgeon, cardiologist, dermatologist, gastroenterologist, physical therapist, mental health nurse, ENT surgeon and a behavior specialist should check up the child right after delivery. Parental education regarding management of Down syndrome is important, as parents need to be aware of the different possible complications associated with it for proper treatment.

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