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DOWN SYNDROME CLINICAL FEATURES, AND IT'S ASSOCIATED COMPLICATIONS EVALUATION AND MANAGEMENT APPROACH

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ABSTRACT

Trisomy 21 (T21), or Down syndrome (DS), is one of the major causes of intellectual disability, this has been analyzed to differ in every individual by the intelligence quotient (IQ) test irrespective of other factors. It is a genetic disorder characterized by an extra copy of chromosome 21. PubMed database was used for searching relevant papers, and the following keys were used in the mesh (("Down syndrome " [Mesh]) AND ("Features and diagnosis" [Mesh]) OR ("Down syndrome Features and diagnosis " [Mesh])). Inclusion criteria were all the articles that consisted of one of the following topics: Down syndrome Features and diagnosis. Concerning exclusion criteria, all articles which did not have one of the inclusion criteria as their topic was not selected. To date, nothing has been developed that effectively improves cognition in children with DS, but effective early stimulation therapy, behavioral intervention, a positive home environment, education, and vocational training are all useful in improving their overall functioning and productivity.

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Introduction

Down syndrome (DS) is one the most common distinguishable genetic cause of intellectual disability seen in general practice. The disability was named after British physician John Langdon Down, who enumerated the physical stigmata of the syndrome in 1866 [1]. Down syndrome was thought to be associated with late pregnancy until trisomy 21 was identified as the underlying cause [2]. The general incidence ranges from 1 per 800–1,200 live births around the globe. The incidence of Down syndrome is not associated with religion, identity, race, or socioeconomic status. Over the last three decades, improved care and early management of complications have greatly improved the overall life expectancy of individuals with DS, and recent research has managed to point to the region of the 21st chromosome responsible for producing the phenotype of Down syndrome [3]. Indeed, up until recently, children with Down syndrome were believed to be of limited ability and lifespan and were placed in institutions to live out their lives.

Epidemiology

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Down syndrome is a common genetic condition that is caused when there is an additional copy of chromosome 21. Indeed, humans normally inherit 46 chromosomes, half from each parent, unlike people with down syndrome who inherit 47 chromosomes due to an additional copy of chromosome 21. This additional DNA causes developmental issues and physical characteristics commonly associated with the syndrome [4].

Although Down syndrome is more common among babies born to older mothers, the extra copy of chromosome 21 is acquired by chance and any mother may have a baby with the condition.

There are three different types of Down syndrome, but all display similar behavioral and physical features: babies born with a whole separate extra copy of chromosome 21 (In about 95% of cases), babies born with a part of a whole extra copy of the chromosome attached to another chromosome rather than existing as a separate copy (In around 3% of cases), and "mosaic Down syndrome" where an extra copy of chromosome 21 can be found in a fair amount but not all of the baby's cells (in around 2% of cases). Studies have also shown that the father's older age also increases the risk of Down syndrome when the mother is aged over 35, but not if she is under 35 [4].

Materials and Methods

PubMed database was used for searching relevant papers, and the following keys were used in the mesh (("Down syndrome " [Mesh]) AND ("Features and diagnosis" [Mesh]) OR ("Down syndrome Features and diagnosis " [Mesh])).

Inclusion criteria were all the articles that consisted of one of the following topics: Down syndrome Features and diagnosis.

Concerning exclusion criteria, all articles which did not have one of the inclusion criteria as their topic was not selected.

Around 90 publications were chosen as the most clinically relevant out of 1,202 articles indexed in the previous two decades, and their full texts were evaluated. A total of 31 of the 90 were included after a thorough examination. Additional research and publications were found using reference lists from the recognized and linked studies. Expert consensus recommendations and commentary were added where relevant to help practicing physicians assess chest pain most simply and practically possible.

Results and Discussion

The genetic condition vastly responsible for the majority of Down syndrome comes together with nondisjunction (NDJ), which is the nonseparation of chromosome 21 (Ch21) either at an early phase of embryonic development (postzygotic NDJ) or at parental gametogenesis (meiotic NDJ) [5]. Indeed, errors in oogenesis during the first maternal meiotic division account for the vast majority of babies with trisomy 21, which characterizes women at an older stage of reproduction as a greater risk factor for DS. Indeed, having a pregnancy after 35 years increases the risk of DS, and the risk increases proportionally to increasing maternal age [6]. The association between full trisomy 21 and the mother's age at conception has been confirmed in studies that were replicated over different periods and in several different populations, thereby placing maternal age as the only risk factor of which we are certain for the great majority of DS pregnancies [7].

Another risk factor for chromosome 21's nondisjunction (MDJ) during meiosis is recombination errors [8]. Particularly, Meiosis I errors (MI errors) have been tied to the absence of recombination or the presence of a single event near the telomere of 21q, unrelated to the age of the oocyte [9]. MII errors, however, have been tied to the recombination occurring near the centromere of 21q thus correlating with the age of the oocyte [10].

There are other risk factors associated with the advanced reproductive age of a woman in having a child with trisomy 21. Indeed, even though several studies tend to focus on chromosome recombination patterns, impaired folate metabolism, and maternal age, other likely risk factors have been investigated. These include socioeconomic conditions, the use of contraceptive pills, cigarette smoking radiation exposure, and maternal weight during pregnancy [11]. Indeed, to improve the accuracy of screening tests, serum markers should be adjusted for appropriate detection of a possible trisomy 21 for maternal weight because it will cause the concentrations of maternal serum markers to change. There is a higher risk of birth of a child with DS tied to maternal obesity [12].

The paucity of available oocytes from mothers of DS infants constitutes the maximum study of the molecular mechanisms that are primary to chromosome 21 missegregation. Several studies looking to investigate other maternal risk factors have been done in surrogate cells and tissues, including peripheral lymphocytes from females who were born a child with DS at a younger age than that which is considered high risk [13].

Symptoms and Signs

Carrying a child with Down syndrome does not involve any symptoms outside of a normal pregnancy, but the likelihood of carrying a child with DS can be screened.

The diagnosis of Down syndrome can be made at birth upon physical examination. Infants will present with [14]:

- Microcephaly, with flattening of both the occiput and face
- Recessed nose, eyes upwardly slanted with epicanthal folds and, occasionally, Brushfield spots
- Small ears and mouth, as well as bulging tongue
- Broad and stocky neck, with loose skin, folds at the nape
- Funnel-shaped chest

- Small and stubby feet, hands, and digits with brachyclinodactyly of the 5th digits, often with a single palmar crease on the palms
- Poor muscle tone

Even when the diagnosis appears straightforward, chromosome analysis should be done to rule out translocation or mosaicism [14]. An infant with DS will be born the same size as any other infant, but physically will develop more slowly. People with Down syndrome usually have a mild to moderate level of developmental disability. Delays are both mental and social [14], which can suggest that the child will display poor judgment, impulsive behavior, reduced focus, and diminished comprehensive capabilities [14]. Down syndrome usually has accompanying complications. These may include hearing loss, poor vision, cataracts, chronic constipation, sleep apnea, late tooth growth causing problems with chewing, obesity, congenital heart defects, hip problems, leukemia, dementia, and Alzheimer's disease, and hypothyroidism. Patients with DS are also at increased risk of infection and regularly suffer from skin conditions, respiratory infections, and urinary tract infections [14].

Diagnosis

The preferred standard for the diagnosis of Down syndrome, although it is mainly clinical, remains the chromosomal analysis bringing the extra copy of chromosome 21 to light. Molecular cytogenetic testing methods like quantitative fluorescent polymerase chain reaction (QF PCR) and interphase fluorescence in situ hybridization (FISH) are rapid and useful for small or premature neonates suspected of having DS [15].

Another useful test that detects the likelihood of babies being born with Down syndrome is Antenatal screening. Indeed, antenatal screening is recommended for women of all age groups according to the American College of Obstetrics and Gynecology (ACOG) and the American College of Medical Genetics (ACMG) [16], either in the first trimester or the second. The detection rate of the first-trimester screen varies between 80 % and 82 % at a false positive rate of 3 % [17]. As for the second-trimester screening, if combined with an 18-week anomaly scan, the detection rate is approximately 80 % at a false positive rate of 3 % [17] and a quadruple test is usually referred to as a triple test. If the risk for Down syndrome exceeds 1:250, prenatal diagnosis may be offered to examine the fetal chromosomes, either by chorionic villi sampling at 11/12 weeks or amniocentesis at 16/18 weeks [17].

Treatment

There is no cure for Down syndrome. However, today, individuals can live a happy, healthy, and relatively independent life provided that they are engaged in the following:

1. Initiation of early stimulation or intervention to improve their overall developmental skills
2. In a good home environment and parental care
3. Participation in education and parental support groups to share their experiences
4. Appropriate and specialized medical care through all ages

Developmental and behavior are highly dependent upon associated co-morbidities, home environment, socioeconomic status, and the education level of the parents. Early stimulation therapy and behavioral intervention has been proven to improve long-term outcome and is the most important management tool for children with Down syndrome. Parents need to be involved in individualizing the training program, identifying and managing behavioral deficits, and maximizing self-help skills to encourage possible independence. Such programs consist of physiotherapy, occupational therapy, and speech therapy [18]. Some experts believe that the earlier stimulation therapy starts, the better chance at good developmental quotients (DQ) and the more likely it will be in reducing further costs of rehabilitation and specialized schools, as well as parental frustration [18] Specialists have been known to prescribe therapeutic dietary supplements to improve cognition in children with DS; however, no scientific evidence points to any combination of drugs, vitamins, or minerals that enhance either psychomotor development or cognitive function in people with DS [19]. Drugs such as Donepezil [20] (a reversible acetylcholinesterase inhibitor) and Rivastigmine [21] have been studied for possible effects on language performance and cognition in children with DS but thus far neither of them have proved to have any effect, though they were well tolerated. Larger, randomized studies of these drugs with a longer follow-up would be necessary to confirm the absence of results in children with DS [18].

Conclusion

To date, nothing has been developed that effectively improves cognition in children with DS, but effective early stimulation therapy, behavioral intervention, a positive home environment, education, and vocational training are all useful in improving their overall functioning and productivity. Regular monitoring and early discovery of possible medical complications are steps taken to decrease the chances of overall morbidity, resulting in more positive outcomes.

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