

Obesity in Youth with Down Syndrome

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Abstract

Introduction: Down syndrome is the most prevalent genetic disorder and, also, the commonest genetic cause of intellectual impairment. Obesity has been addressed as a major public health problem, particularly, among individuals with Down syndrome.

Aim of Work: This is an overview of related obesity prevalence in youth with Down syndrome and the different aspects of its risk factors.

Methodology: A comprehensive and systematic search was conducted regarding different obesity in individuals with Down syndrome. MEDLINE, Google Scholar, Cochrane Library, and Embase engines were the mainly used database.

Conclusion: Obesity among youth with Down syndrome have high prevalence of 23 - 70%. Patients with Down syndrome demonstrated significantly greater prevalence of obesity when compared to unaffected relatives. Obesity rates increase after age 2 years in children with Down syndrome. Youth with Down syndrome may have low-nutrient intake, but an association between energy-dense and low-nutrient food intakes and obesity has not been entirely established.

Keywords: Obesity; Down Syndrome

Introduction

Down syndrome is the most common chromosomal disorder with prevalence ranges from 6.1 to 13.1 per 10,000 people [1,2]. During the last century life, expectancy among persons with Down syndrome has increased [1]. Increased life expectancy could be linked to growing governmental and non-governmental initiatives, as well as improvements in medical care and services for persons with Down

syndrome [3]. Despite such improvements, challenges still exist for establishing health care services for children with Down syndrome worldwide. These challenges are linked to several conditions including congenital heart defects, hearing dysfunctions, gastrointestinal disorders, thyroid disease, cognitive impairments, and obstructive sleep apnea [4,5]. The American Academy of Pediatrics and the U.S. Government for has been addressing public health research and health care, highlighted obesity as another risk to the health aspects of individuals with Down syndrome [4,6]. This literature review aim was to examine the obesity prevalence in youth with Down syndrome from birth to age 20 years and to examine differences in weight status between youth Down syndrome and youth without Down syndrome.

Methods

We ran a systematic search in MEDLINE, Google Scholar, Cochrane Library, and Embase. Using each database's internal thesaurus (e.g. [MeSH] in MEDLINE), we designed the search approach into several aspects for ease of search-Down's syndrome, obesity, body mass index (BMI); overweight; weight; body fat; body composition; and skinfold thickness.

Prevalence of overweight and obesity

Obesity among youth with Down syndrome have high prevalence of 23 - 70%. Few studies featured a comparison of the prevalence of obesity between youth with Down syndrome and youth without disabilities [7,8]. Patients with Down syndrome demonstrated significantly greater prevalence of obesity (BMI-for-age \geq 95th percentile) when compared to unaffected relatives [8]. Van Gameren and his colleagues reported an increased rates of overweight and obesity in 659 youth with Down syndrome than the general population [9]. Further insight into overweight and obesity in youth with DS was demonstrated in studies comparing mean BMI between youth with and without Down syndrome. These studies found higher BMI in youth with Down syndrome [8,10-12].

Gender differences

Two large retrospective population-based studies from the Netherlands and Sweden offer information regarding gender differences in overweight and obesity among youth with DS [13]. These studies suggested a higher prevalence of overweight in females, but they lack a statistical analyses between genders. Gonzalez., *et al.* reported a substantially higher BMI in the girls [14]. These reports collectively suggest a higher body weight status in girls than boys with Down syndrome. However, gender has not been identified as a risk factor for obesity among youth with Down syndrome.

Age differences

Recent studies have aimed to identify the age period for the development of obesity in youth with Down syndrome. These studies reported that youth with Down syndrome tend to have higher rates of overweight and obesity from 2 years of age [15]. In a retrospective cohort study, Alexander and his colleagues reported that the incidence of obesity was elevated at all ages [16]. Further, individuals with Down syndrome, aged 3-6 years and older, demonstrated an incidence rate of 6.8 (95% CI: 4.1 - 11.3). In a cross-sectional study, Grammatikopoulou., *et al.* reported higher BMI among individuals aged 10 - 18 years than children aged 2 - 9 years (BMI z-score of 1.45 ± 0.71 and 0.06 ± 1.45 , respectively) [17]. Collectively, these findings indicate that the obesity rates increase after age 2 years in children with Down syndrome, but further investigation towards identifying the critical periods for becoming overweight or obese during adolescence, which would be of significance helpful to parents and clinicians for implementation interventional measures.

Identified determinants

Attempting to explain the expanding epidemic of childhood obesity, many hypotheses have been proposed, involving a multiple of biological and environmental factors.

Leptin

Leptin is a hormone produced by the adipose tissue. Labeled as the “satiety hormone”, this hormone regulates energy balance by inhibiting hunger. Studies has demonstrated an association between higher serum leptin levels in obese subjects and increased leptin resistance. However, the causation has not been entirely established [18,19] than relatives without Down syndrome, suggesting that leptin in youth with Down syndrome may be elevated for factors other than body composition [10]. Inconsistently, Yahia., *et al.* found that there was no significant different between obese children with Down syndrome and obese children without Down syndrome [20]. However, this study reported that obese children with Down syndrome showed higher leptin levels than non-obese children with DS. These findings suggests that the mechanism of leptin resistance may be involved when considering that high levels of leptin and obesity coincide in youth with Down syndrome.

Resting energy expenditure (REE)

High prevalence of obesity have directed researchers to hypothesize that lower resting energy expenditure may to some extent explain the increased risk of obesity in youth with Down syndrome. Hill and his colleagues reported that children with Down syndrome aged 3 - 10 years showed lower REE compared to siblings without DS [8]. Further, this difference continued even after an additional adjustment for fat mass, sex, and race. This study found that resting energy expenditure was not associated with fat mass changes over three years. In addition, a cross-sectional study reported a moderate correlation between %BF and resting energy expenditure in youths with Down syndrome aged 10 - 14 years [21]. Collectively, the existing results consistently demonstrate that children with Down syndrome tend to have lower REE than siblings without DS. However, low resting energy expenditure has not been directly addressed as a causative element for obesity among these youths.

Physical activity (PA)

Energy balance is affected by physical activity. Low PA may significantly contribute to obesity in youth with Down syndrome, as it has been suggested for youth without DS [22]. It appears that youth with DS have lower physical activity levels than siblings without Down syndrome [23]. Further, it has been suggested that PA may decrease with age in youth with Down syndrome [23]. Therefore, these factors may potentially lead to the high obesity rates in youth with Down syndrome. A cross-sectional study reported that physical activity had weak association with BMI and %BF in 104 U.S. youth with Down syndrome aged 8 - 16 years [24]. A study in children without Down syndrome have suggested that physical activity has minor impact on fat loss [25]. However, this might be attributed to methodological obstacles such as study designs, statistical measures used, and techniques accuracy in estimating adipose tissue and physical activity [26].

Nutrition

Studies have established the relationship between overweight and consumption of energy-rich food in the population of general childhood [27]. There is lack of studies examining this issue extensively in youth with DS. Unonu and Johnson found a significant positive correlation of energy intake with skinfold of triceps, but not with body weight among children with Down syndrome aged 2 - 6 years [28]. Also, the same study results showed some micronutrient deficiencies; namely, vitamin B-6, folate, zinc, iron, and calcium. In contrast, another study among only 10 youth with Down syndrome reported that those who were not obese were more liable to have micronutrient deficiencies than those who were obese [29]. Deficiencies in vitamins and minerals could be attributed to excessive consumption of energy-rich, refined, and micronutrient poor foods. These results suggest that youth with Down syndrome may have low-nutrient intake, but an association between energy-dense and low-nutrient food intakes and obesity has not been entirely established.

Comorbidities

The association between the increased risk of obesity in children with DS and comorbidities, especially thyroid diseases and heart defects. Oosterom., *et al.* reported that no significant differences in overweight rates between healthy children with Down syndrome

and those with hypothyroidism and heart defects [9]. Another study found that Down syndrome youth with hypothyroidism showed decreases in BMI after L-thyroxine treatment. Also, those with heart defects had higher BMI than children with DS without defects [30].

Consequences

There has been some hypotheses that link the weight status of youth with Down syndrome with adverse health outcomes. These conditions includes obstructive sleep apnea, dyslipidemia, hyperinsulinemia, biomechanics complications and impaired cardiorespiratory fitness.

Obstructive sleep apnea (OSA)

Individuals with Down syndrome are more liable to have severe obstructive sleep apnea than the general population [31]. Studies found that obstructive sleep apnea was associated with weight [32-34]. Ng and his colleagues reported that, among 22 Down syndrome children, 31.2% were obese. Also, apnea-hypopnea index was significantly related with weight-for-age. Some studies have supported the hypothesis that physical status could predispose persons with Down syndrome to obstructive sleep apnea due to their smaller upper airway, adenoid hypertrophy, lingual tonsillar hypertrophy, and muscular hypotonia [31,33]. The existing data suggest that obesity may potentially contribute to obstructive sleep apnea in youth with Down syndrome.

Dyslipidemia

Dyslipidemia is more likely to be prevalent among obese children than normal weight children [34]. In youth with Down syndrome, cross-sectional studies examined the association between weight status with total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides. In the study by Ordonez and his colleagues found higher BMI and waist-to-hip ratio were correlated with higher triglycerides and lower levels of HDL in Spanish children with Down syndrome aged 16 ± 1 years. Another study showed that healthy children with Down syndrome aged 4 - 10 years had abnormal lipid profiles when compared to siblings [35]. Though these findings suggest that youth with Down syndrome have less favorable lipid profiles, obesity has not been addressed as a risk factor for dyslipidemia in DS population.

Hyperinsulinemia

It has also been suggested that obese youth with DS have increased risk of hyperinsulinemia. In cross-sectional study, 15 Brazilian obese participants aged 10 - 18 years had higher insulin and homeostatic model assessment than those of normal weight [36]. Further, another study reported that obese children with Down syndrome had higher median values of insulin and insulin and homeostatic model assessment compared to non-obese children with Down syndrome [20]. In summary, Most research in children addresses obesity as an antecedent to [34]. Obesity is linked to insulin resistance leading to hyperinsulinemia, suggesting that the same applies to youth with Down syndrome [37].

Orthopedic aspects

Youth with Down syndrome have inherent orthopedic alterations, such as flat feet, possibly resulting from hypotonia and laxity of ligaments [11]. Studies have examined the effect of obesity on biomechanics impairment in children with Down syndrome. The relationship between obesity and plantar pressure distribution was assessed in Italian children with Down syndrome aged 3 - 18 years. This study found that obese children with Down syndrome showed significantly greater contact and higher plantar pressures in the forefoot than non-obese children with Down syndrome [38]. Consistently, another Italian study reported that obese youth had longer stance duration and less dorsiflexion during the swing phase than non-obese siblings [39]. Collectively, these results suggest that obesity in children with Down syndrome has a major impact on gait patterns far from that of DS alone.

Cardiorespiratory fitness (CRF)

Individuals with Down syndrome have very low peak oxygen consumption [40]. A review suggested that this could be partially attributed to autonomic difficulties in reaching a high peak heart rate [40]. Recent studies examined the relationship between obesity and cardiorespiratory fitness in youth with Down syndrome. A retrospective study reported lower HR_{peak} and VO_{2peak} in children with Down syndrome compared to youth with and without cognitive disability aged <18 years. However, obesity was not associated with VO_{2peak} or HR_{peak} [41]. In contrast, another study, in individuals with Down syndrome aged 11-20 years, found that fatness had no clear effect on CRF [42]. Therefore, this limited existing knowledge highlights the notion that cardiorespiratory fitness is low in youths with Down syndrome and that obesity is not a significant risk factor for impaired cardiorespiratory fitness in these children.

Conclusion

Obesity among youth with Down syndrome have high prevalence of 23 - 70%. Patients with Down syndrome demonstrated significantly greater prevalence of obesity when compared to unaffected relatives. Obesity rates increase after age 2 years in children with Down syndrome. Youth with Down syndrome may have low-nutrient intake, but an association between energy-dense and low-nutrient food intakes and obesity has not been entirely established. Also, obesity is linked to insulin resistance leading to hyperinsulinemia, suggesting that the same applies to youth with Down syndrome. In addition, obesity may potentially contribute to obstructive sleep apnea in youth with Down syndrome. Cardiorespiratory fitness is low in youths with Down syndrome and obesity is not a significant risk factor for impaired cardiorespiratory fitness in these children.

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