ESPE Physician Information Leaflet on COVID-19 and Pediatric Endocrine Diseases

Disease specific information and advice: OBESITY

Introduction

Infection by coronavirus 2 (SARS-CoV-2) can lead to disease COVID-19, a flu-like illness. On January 3, 2020, a novel coronavirus—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 or 2019-nCoV)—with phylogenetic similarity to the SARS coronavirus (SARS-CoV), the cause of the 2003 SARS outbreak, was isolated in samples of broncho-alveolar lavage fluid from patients in Wuhan and was confirmed as the cause of the novel atypical form of pneumonia (Lu 2019). On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a public health emergency of international concern (WHO march2020). The most recent prevalence figures can be found on the website of the European center for disease control (https://www.ecdc.europa.eu/en/covid-19-pandemic). The virus spreads like any other respiratory infectious disease, through contaminated air-droplets of infected persons when talking, coughing, or sneezing. It can survive in the environment from a few hours to a few days, depending on surfaces and environmental conditions. The mouth, nose, and ocular mucosa appears to be the major source of transmission. Children account for 1-5% of diagnosed COVID-19 cases (Ludvigsson 2020). In addition to this, COVID-19 disease course is less severe in children than in adults. (Ludvigsson 2020; Ping-Ing 2020) A study found that more than 90% of laboratory verified or clinically diagnosed children with COVID-19 had asymptomatic, mild or moderate disease. Of the remainder, 5.2% had severe disease and 0,6% had critical disease (Dong 2020).

In this review, we present a brief overview of the current knowledge on COVID-19 and its relationship with obesity in children and adolescents, and we provide recommendations as Pediatric Endocrinologists managing patients with endocrine disorders during the COVID-19 pandemic.

The link between obesity and severe course of COVID19

Several potential pathways link obesity to increased risk of severe course of COVID-19.

1. Angiotensin converting enzyme. Obesity is associated with an imbalance in the renin-angiotensin-aldosterone system (RAAS). This imbalance is characterized by an overexpression of angiotensin 2 (ANG2). ANG2 can be converted to angiotensin 1-7 (Ang1-7) by Angiotensin converting enzyme (ACE2). (Radzikowska 2020). ANG2 has a pro-inflammatory effect, while ANG1-7 has an anti-inflammatory effect. It is therefore likely that this imbalance also contributes to the probability to

develop a pro-inflammatory dysregulated immune response. SARS-CoV-2 enters the host cell by binding to ACE2. This happens mostly in the lungs, however, ACE2 is also expressed in adipose tissue, which is abundant in individuals with obesity. This raises the question whether adipose tissue can be infected by SARS-CoV-2 and could therefore function as a reservoir for viral spread. This could result in prolonged viral shedding, increased viral load, and extended cytokine activation in the already low-grade inflamed adipose tissue. This could increase the probability that obese patients spread virus to others (Ryan 2020).

2. Obesity is linked to underlying impairments, such as type 2 diabetes, hypertension, thrombogenic risk, and lung impairment. These impairments all decrease the ability to cope with COVID-19. (Sattar 2020).
3. Viral shedding. The concept that patients with obesity might have increased viral shedding of SARS CoV 2 comes from studies on the influenza A virus. It was found that obese patients are more contagious than lean patients. This is due to several factors. First, symptomatic obese patients shed influenza A virus 42% longer than lean patients, probably due to their altered immune response (Maier 2018). Second, BMI positively correlates with viral load in exhaled breath. This indicates that obese patients exhale a higher viral load, therefore increasing the probability to infect others (Yan, Grantham et al. 2018). Since SARS-CoV-2 is an influenza-like virus strain, it seems likely that these findings also apply to obese patients infected with SARS-CoV-2 (Luzi 2020).
4. Vaccine effectiveness. Vaccination is the best prevention against viruses. At the moment, the world is waiting for a vaccination against SARS-CoV-2. However, individuals with obesity are known to have a decreased influenza vaccine effectiveness, probably due to alterations in the immune system (Karlsson 2016).). It is possible that this effect can also occur in obese individuals when vaccinated against SARS-CoV-2, leading to decreased prevention of COVID-19 in obese patients.
5. Leptin. Obesity is characterized by higher leptin levels and lower adiponectin. Leptin is a pro-inflammatory adipokine, while adiponectin is an anti-inflammatory adipokine (Luzi, Radaelli 2020). In addition to this, leptin has an immune regulative role. High amounts of leptin cause a decrease in regulatory T (Treg) cells and an increase in pro-inflammatory type 1 T-helper (Th1) cells. This contributes to the chronic low-grade inflammatory state and likely increase the probability of a SARS-CoV-2 induced dysregulated immune response as well (Rebello 2020).

Are children with obesity predisposed to a more severe course of obesity?

Obesity is a risk factor for increased COVID-19 severity in adults. This raises the question whether this relation also accounts for children. A patient cohort study in New York found that obesity was associated with mechanical ventilation in their COVID-19 children ≥2 years. (Zachariah, Johnson et al.

2020) In another study, obesity was highly prevalent among COVID-19 positive tested children. However it has to be noted that in this study, a higher number of severe cases was found than previously recorded and the general prevalence of obesity was not registered. (Chao 2020). In adults, several co-morbidities are associated with increased COVID-19 severity, these conditions include cardiovascular diseases, hypertension, type 2 diabetes, and obesity. Most of these are not common in children, therefore placing children in a favorable position against COVID-19. Several comorbidities of obesity increase the risk of severe COVID-19, such as hypertension and type 2 diabetes) (Ebbeling 2002). A study found that 23% of the children that needed invasive ventilation had obesity and/or type 2 diabetes (Shekerdemian 2020; Kass 2020). This shows that obesity and its comorbidities play a role in COVID-19 severity in both adults and children.. These studies suggest that obesity is a risk factor for increased COVID-19 severity in children. However, the absolute risk is still very low compared to the increased risk in adults with obesity, since the number of severe COVID-19 cases is generally low in all children, including children with obesity.

Corona measures are not different for children/adolescents with obesity than for the general population.

Adhering to the general rules for the protection from the coronavirus, including social distancing, thorough hand washing, and avoidance of face touching and meticulous disinfecting of surfaces, is warranted.

How are children with obesity affected by quarantine measures?

To mitigate the spread, several countries have implied measures, such as closing schools, quarantine measures and social distancing. The COVID-19 measures seem to be a more significant health threat to children with obesity than the disease itself. Studies report adverse effects on psychological wellbeing such as anxiety, worrying, irritability, depressive symptoms and post-traumatic stress disorder symptoms in 19- 44% of children from the general population in Asian, European or America. (Xie 2020, Zhou 2020, Chen 2020, Jiao 2020, Orgilés 2020, Qi 2020, Chen2020, Duan 2020) In addition, children with obesity seem to perceive themselves to be vulnerable to COVID-19 because obesity is a risk factor. In a Dutch study among children with severe obesity, age 7-15 years, COVID-19 related anxiety was reported in 32% of children. (Abawi 2020) Self-imposed strict quarantine measures were present in 25% of these families. Quarantine effects on lifestyle was observed in an Italian study showing unfavorable changes in eating, sleeping and activity behaviors in children and adolescents with obesity. (Pietrobello 2020)

Many children experience changes in their home situation, physical activity, sedentary activity, sleep and eating behavior. Since childhood obesity is a complex problem, several of these changes could decrease treatment effectiveness and increase the risk of developing comorbidities. Maintaining a healthy lifestyle by engaging in physical activity even indoors and making healthy food choices are strongly encouraged. Ongoing monitoring of obesity in children/ adolescents is important to maintain during quarantine.

Summary

Obesity is a risk factor for increased COVID-19 severity in children. However, the absolute risk is still very low compared to the increased risk in adults with obesity, since the number of severe COVID-19 cases is generally low in all children, including children with obesity. Corona measures are not different for children/adolescents with obesity than for the general population. The quarantine measures seem to be a more significant health threat to children with obesity than the disease itself. Maintaining a healthy lifestyle by engaging in physical activity even indoors and making healthy food choices are strongly encouraged. Ongoing monitoring of obesity in children/ adolescents is important to maintain during quarantine.

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