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Childhood obesity and SARS-CoV2: dangerous liaisons

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ABSTRACT

BACKGROUND: Nowadays obesity and Coronavirus Disease-19 (COVID-19), for some extent, represent two major public health problems worldwide. These diseases, albeit extremely different, have a pandemic pattern of diffusion and have enormous direct and indirect effects both on health and lifestyle.

AIM: Aim of our narrative review was to analyze in the pediatric population, the relationship between these two diseases using a holistic approach.

MATERIALS AND METHODS: We performed a quasi-review with a systematic literature search through the Cochrane Library and Medline/PubMed databases from 1 January 2013 to 1 October 2020. Two authors independently extracted data using predefined data fields and rated study quality. Two main key words were considered, obesity and COVID-19, pointing a particular focus on pediatric patients. We also analysed the relationship between obesity and COVID-19 in adults for comparison.

CONCLUSION: Evidences showed that during quarantine due to COVID-19, children and adolescents were physically less active, have much longer screen time exposure, sleep patterns disturbances, and less favorable diets, possibly resulting in weight gain and in a loss of cardio-respiratory fitness. Such negative effects on health are likely to be much worse in subjects that are overweight or have obesity. Moreover, stressors emerging from the prolonged national lock-down around the world and from social distancing could have even more problematic and enduring effects considering that obese children are more susceptible to psychiatric disorders. Obesity represents also a risk factor for COVID-19 severity in younger adults but at the moment in pediatric population we have very limited data. Public health interventions are urgently called in order to promote an active lifestyle and engagement in social activities in children and possibly to mitigate the adverse impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in pediatric subjects that are overweight or have obesity.

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KEYWORDS children; overweight; pediatric obesity; co-morbidities; COVID-19; SARS-CoV2

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Introduction

We collected data from December 2019 to June 2020. Our end point is to analyze possible direct and indirect links between COVID-19 and obesity in children and adolescents.

At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. In the following months, this virus produced the pandemic affecting the whole world (Hoffmann et al. 2020; Xu et al. 2020). The World Health Organization (WHO) designated the disease CORonaVirus Disease-19 (COVID-19), and the pathogen that caused it was designated severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a positive single-stranded RNA virus, with a genome of 30 kb which encodes for protein E, envelope, protein S, spike; protein M, membrane; and protein N, nucleocapsid. According to most recent studies, glycoprotein S binds Angiotensin Converting Enzyme 2 Receptor (ACE2-R), which is found primarily in the lower respiratory tract, rather than in the upper airway and exploits the activity of a cellular metalloproteinase (TMPRSS2) (Hoffmann et al. 2020), in order to fuse with host cell membrane and release viral RNA into cytosol (Xu et al. 2020).

In Italy, the first 3 cases were reported in the first half of February 2020 in Lombardy Region, North part of Italy, and were limited to people who had traveled to China in the previous two weeks. Then the cases of COVID-19 began to pop up also in Veneto Region, a close Region to Lombardy, starting from a small town in the province of Padua (Onder et al. 2020). In the following weeks, the infection spread to all the Country, hitting harder in the northern regions of Italy (Onder et al. 2020). According to data of the Istituto Superiore Sanità (ISS) adjourned up to 19 June 2020, SARS-CoV-2 has caused 238.011 cases and 34.561 deaths. The COVID-19 disease can affect all age groups, although children and/or adolescents seem to be less susceptible to this infection. Data on pediatric population showed that between 0 and 9 years of age there, have been 4 deceased patients (3 girls and 1 boy), with a lethality percentage of 0.2%. Between 10 and 19 years there were no deaths, bringing lethality to 0%. Moreover, of the total SARS-CoV-2 positive patients, only 2.0% were between 0 and 18 years old.

Data from Regina Margherita Hospital in Turin (Italy), until 25 April 2020 reported in children 36 cases positive to COVID-19, with an average age of 6.7 years old (SD: 5.54 years). The average Body Mass Index (BMI = kg/m^2) of this population was $17.74 \text{ kg}/\text{m}^2$ (SD: $4.15 \text{ kg}/\text{m}^2$) (Denina et al., personal communication).

The spectrum of symptomatic infection ranges from mild, common cold-like, to critical, with patients having respiratory failure and severe pulmonary involvement. Although, most infections, luckily, are not severe. The most

common symptoms are fever, cough, dyspnea and in some cases watery diarrhea. Another symptom that in adults can be linked to COVID-19 seems to be sudden and complete olfactory function loss (Eliezer et al. 2020). Recently, in a systematic review of 18 studies involving pediatric patients worldwide, Castagnoli et al. (2020) demonstrated that children and/or adolescents undergo less severe COVID-19 infection in general when compared to adults, with mild symptoms and generally good prognosis (Castagnoli et al. 2020).

Mantovani et al. (2020) in a meta-analysis confirmed Castagnoli et al. data (2020), showing also specific percentage of symptoms in 2855, mainly Chinese, children and/or adolescents (mean age 6.9 years, standard deviation 7.0 years; 50.3% males) where the diagnosis of COVID-19 was confirmed by nasopharyngeal swabs (Mantovani et al. 2020). Overall, 47% of children had fever (95%CI:22 – 72%; I2 = 98.6%), 37% cough (95% CI:15 – 63%; I2 = 98.6%), 4% diarrhea (95%CI:0 – 12%; I2 = 92.2%), 2% nasal congestion (95%CI:0 – 7%; I2 = 87.7%), 1% dyspnea (95%CI:0 – 7%; I2 = 91.5%) and 0% abdominal pain (95%CI: 0 – 1%; I2 = 76.3%). Children and adolescents presented mild symptoms in 79% (95%CI:65 – 91%; I2 = 93.5%) of cases, whereas only 4% (95% CI 1 – 9%; I2 = 76.4%) of patients were considered in critical conditions (Mantovani et al. 2020).

In Italy up to now there is another public health problem that is pediatric obesity. This chronic and pandemic disease has a widespread impact also on psycho-social health and lifestyle. The prevalence is continuously increasing both in adult and in pediatric populations and so does the burden of obesity-related disease worldwide. In Italy, Greece and Spain 1 in 5 boys (19–21%) are obese. In Italy 42% of boys and 38% of girls, aged between 6 and 9 years, have a BMI >85th percentile for age and sex.

Almost all children with overweight and subjects with obesity are strongly influenced by environmental factors that consequently represent important targets for treatment being potentially modifiable. Pietrobelli et al. (2020), in a longitudinal study reported that youths with obesity, when removed from structured school activities and confined to their homes during the COVID-19 pandemic, displayed unfavorable trends in lifestyle behaviors (Pietrobelli et al. 2020). Pietrobelli et al., showed increasing trends in glycemic index of foods, sugar-containing drinks, including fruit juice, potato chips, screen watching (i.e. computers, televisions, smartphones, tablets) and decreasing structured physical activity (Pietrobelli et al. 2020). It is very well known that the amount of time spent watching television or the presence of a television in a child's bedroom are directly related to the prevalence of pediatric obesity (Gilbert-Diamond et al. 2014). These effects are probably due to a depression of metabolic rate, displacement of physical activity, adverse effects on diet quality, the lost of an appetite-driven food consumption and effects on sleep (Gilbert-Diamond et al. 2014).

Table 1. Obesity and overweight related co-morbidities.

Psychosocial:	Social isolation, anxiety, depression, distorted peer relationship, disordered eating patterns
Cardiovascular:	Hypertension Dyslipidemia Abnormal cardiac structure and function Premature atherosclerotic cardiovascular disease
Endocrine:	Prediabetes, diabetes mellitus Metabolic syndrome Hyperandrogenism and polycystic ovary syndrome Precocious puberty Exposure to endocrine disruptors
Gastrointestinal:	Non alcoholic fatty liver disease Cholelithiasis
Orthopedic:	Slipped capital femoral epiphysis Genu varus or valgus Fractures
Pulmonary:	Asthma, Respiratory Obstructive Syndrome
Renal:	Albuminuria, impaired kidney function

Several co-morbidities are related to pediatric overweight and obesity (Table 1). All of them are playing a role in the lifestyle having psychosocial consequences together with overweight and obesity *per se*. Keeping in mind these two major problems at the moment, COVID-19 pandemic and pediatric obesity we looked at articles with data on COVID-19 with also information on obesity status in order to see if these two diseases could have something in common or could influence each other.

Material and methods

We performed a quasi-review with a systematic literature search through the Cochrane Library and Medline/PubMed databases from 1 January 2013 to 1 October 2020. Two authors independently extracted data using predefined data fields and rated study quality. Two main key words were considered, obesity and COVID-19, pointing a particular focus on pediatric patients. We also analysed the relationship between obesity and COVID-19 in adults for comparison.

Discussion

Nowadays pediatric obesity and COVID-19 represent two major public health problems worldwide. These diseases, albeit extremely different, have a pandemic pattern of diffusion and have enormous direct and indirect effects both on health and lifestyle. Indeed, this global viral pandemic is also becoming a global economic crisis which will disproportionately affect the world's most vulnerable population that is precisely the one at higher risk of obesity.

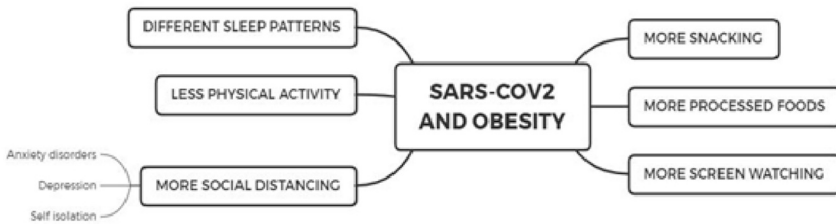


Figure 1. Indirect effects between Sars-CoV2 and obesity.

Since March 10th, 2020, Italy has been a red zone and nearly 10 million children and adolescents have been isolated at home. Indirectly this situation might contribute to worsen the obesity crisis in the future, also with regards to pediatric patients, as weight loss programs and interventions are being severely curtailed. Moreover, the need for self-isolation is prompting many families to rely on processed foods with longer shelf life and canned foods with higher quantities of sodium. A longitudinal study by Pietrobelli et al. (2020), concretely showed unfavorable changes in eating, activity and sleep behaviors in pediatric patients with overweight during quarantine in Verona (Pietrobelli et al. 2020). Obviously, the social distancing and stay-at-home orders issued in cities across the globe reduce the opportunities for physical activity among children, particularly for children in urban areas living in small apartments. Sedentary activities and screen time are expanding under social distancing orders. Screen time is a well-known risk factor associated with experiencing overweight/obesity in childhood, likely because of the dual issues of sedentary time and the association between screen time and snacking (Robinson et al. 2017). Figure 1 depicts the indirect effects of the association between COVID-19 and obesity in pediatric population.

On the same line, Rundle et al. (2020) argued that COVID-19 pandemic, by restricting children from attending school, exacerbated the risk factors for “... weight gain associated with summer recess ...” (Rundle et al. 2020). An easily neglected issue is the psychological impact on children and adolescents. Stressors such as prolonged duration, fears of infection, frustration and boredom, inadequate information, lack of in-person contact with classmates, friends, and teachers, lack of personal space at home, and family financial loss, could have even more problematic and enduring effects on children and adolescents (Wang et al. 2020). Sprang and Silman (2013) showed that the mean post-traumatic stress scores were four times higher in children who had been quarantined than in those who were not quarantined (Sprang and Silman 2013).

An et al. (2020), using a microsimulation model, simulated the trajectory of a nationally representative kindergarten cohort’s BMI and childhood

obesity prevalence from April 2020 to March 2021 under the control scenario without COVID-19 and under the 4 alternative scenarios with COVID-19- Scenario 1: 2-month nationwide school closure in April and May 2020; Scenario 2: Scenario 1 followed by a 10% reduction in daily physical activity in the summer from June to August; Scenario 3: Scenario 2 followed by 2-month school closure in September and October; and Scenario 4: Scenario 3 followed by an additional 2-month school closure in November and December. Relative to the control scenario without COVID-19 showed that Scenarios 1, 2, 3, and 4 were associated with an increase in the mean BMI (An 2020).

Direct effects and significant links between COVID-19 and obesity are currently not present in the pediatric population but in younger adults there seem to be an important correlation mainly due to inflammatory pathways (Luzi and Radaelli 2020). Luzi et al. (2020), in adults, explored the relationship between influenza and obesity, and showed that higher levels of leptin, alpha-TNF, and IL-6 impair both innate immunity and adaptive immunity (Luzi and Radaelli 2020). In fact, macrophagic activation secondary to antigen presentation is less effective in a pro-inflammatory micro-environment, causing also a blunted response in cytokines, and more specifically IFN-gamma production (Luzi and Radaelli 2020).

The US Center for Disease Control and Prevention (CDC), since an article from Tartof et al. came out in august 2020, lists “severe obesity” as a risk factor for serious COVID-19 illness (Tartof et al. 2020). Mechanisms are likely to be multifaceted, particularly since obesity itself is the result of a complex interaction between genetic, hormonal and environmental factors. Obesity could have a significant impact on mechanical lung function leading to a restrictive spirometric pattern (Cost et al. 2014). It is clearly more difficult to intubate or to perform imaging in patients with obesity. Moreover, as mentioned before, overweight results in a chronic state of inflammation which can impair the immune response.

Simonnet et al. (2020), found that in almost half of 124 patients admitted to an intensive care unit (ICU) with COVID-19 and BMI in the obese range ($>35 \text{ kg/m}^2$) the need for mechanical ventilation increased with increasing BMI (Simonnet et al. 2020). Lighter et al. (2020), in 3,615 subjects positive for COVID-19, found that patients aged under 60 years with a BMI between 30 and 34 were almost twice as likely to be admitted to ICU compared with patients with a BMI less than 30 (Lighter et al. 2020). Petrilli et al. (2020), in a retrospective analysis, described outcomes of people admitted to hospital with COVID-19 and the clinical characteristics associated with severity of illness (Petrilli et al. 2020). The strongest risk for hospital admission was associated with age with an odds ratio of >2 , but the second risk was any increase of BMI with odds ratio of 2.6 (Brambilla et al. 2020).

COVID-19 data in the pediatric population are too limited in order to make a hypothesis regarding possible direct link with obesity. Although, this direct relationship could be expected. Brambilla et al., described a case of 14 years old boy, with a BMI 34 kg/m² developed a severe case of COVID-19 with admission to Pediatric Intensive Care Unit (Lighter et al. 2020). Of course, it is not easy to disentangle cause and effect, although obesity could exacerbate COVID-19 and *vice versa* (Brambilla et al. 2020).

This study was substantially a quasi review of existing literature and so it doesn't allow drawing conclusions whether a link between COVID-19 and Pediatric Obesity actually exists, but only underlines a series of potential risks the combination of these two issues brings. Another limitation was time: this review assembled literature up to October 2020, and could use raw data ranging approximately to six or seven months old at the time of publication, thereby excluding the period of the second wave of contagion, spanning exactly from October to current date. This latter limit is particularly relevant given the fact that COVID-19 is a previously unknown virosis, of which much is yet to be discovered.

Furthermore, the raw data we could collect regard a small population, and more studies are needed in order to better qualify and define the risks these two pathologies combined determine among children and adolescents.

Conclusions

COVID-19 infection could have an important and indirect effect on the physical and mental health of children and adolescents. Evidences show that during quarantine pediatric subjects were in general physically less active, have much longer screen time, irregular sleep patterns, and less favorable diets, with possibly resulting in weight gain and in a loss of cardio-respiratory fitness. Such negative effects on health are likely to be much worse in subject that were overweight or with obesity (Gilbert-Diamond et al. 2014; Robinson et al. 2017; Pietrobelli et al. 2020). On the other hand, it is well known that children with obesity could experience psychiatric disorders more than normal weight peers (Topçu et al. 2016). Stressors emerging from the prolonged national lockdown and from social distancing could have even more problematic and enduring effects. To confirm this hypothesis, Pecoraro et al. (2020), described some interventions to avoid the risk of physical and psychological repercussions in pediatric age enhancing the role of parents, schools and psychologists (Pecoraro et al. 2020).

In adults, obesity condition was found directly related to the severity of COVID-19 and was reported as one of the most prominent risk factors increasing mortality (Tartof et al. 2020). In this scenario, nutritional status and diet might influence individual risk for the progression of COVID-19 severity, but information on pediatric population is still very limited. Public health interventions are urgently called if we wish to promote an active lifestyle and engagement in social activities among children in order to

mitigate the adverse impact of COVID-19 on obesity status.

Aknowlegments

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Disclosure statement

The authors declared no conflict of interest.

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