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REVIEW ARTICLE

## Consequences of COVID-19 on Pediatric Obesity and Endocrinopathies: A Review of the Literature

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### Abstract

The COVID-19 pandemic has impacted children from Kindergarten through 12<sup>th</sup> grade in numerous ways. Strategies aimed at mitigating the spread of the virus early on, predominately social distancing and isolation, negatively impacted children's physical health by limiting access to physical education and facilitating sedentary lifestyles. These negative effects have longstanding implications on the physical health of pediatric patients, and it is especially pertinent to understand these effects during an already alarming pediatric obesity epidemic. As with obesity in adults, obesity in children is associated with numerous endocrine comorbidities. Through a literature review, this paper aims to go beyond understanding how the COVID-19 pandemic negatively impacted the physical health of children and describe how the pandemic may have long-term effects on childhood obesity and endocrinopathies in pediatric patients. Additionally, it describes the direct impact COVID-19 may have on the increased incidence of endocrinopathies in pediatric patients.

## Introduction

Lockdowns secondary to the COVID-19 pandemic were first introduced three years ago in March 2020. They were implemented to slow the spread of the virus, and they have impacted nearly every aspect of life. Children were removed from their classroom environments and transitioned to online learning platforms to continue their education. However, some aspects of school life were more difficult to transition with pandemic restrictions. Notably, physical education and school lunches experienced the most disruption.

The incidence of childhood obesity has continued to rise over the past decade and is now at an all-time high.<sup>1</sup> Consequences of this epidemic in children are both immediate and distant in the form of endocrinopathies, cardiovascular consequences, and anxiety and depression.<sup>2,3,4</sup>

This paper seeks to review the consequences of COVID-19 on childhood obesity and endocrinopathies in pediatric patients. The impact on obesity will be presented as a review of how the pandemic led to increased caloric intake, increased sedentary behaviors, and decreased physical activity. The impact on endocrine pathology will be reviewed as both direct impacts of the virus and indirect impacts secondary to pandemic lockdown measures. Our conclusion will address steps moving forward to protect the most vulnerable populations who experience the effects of the pandemic, childhood obesity, and endocrinopathies from multiple perspectives.

## Physical Health

As an overview, obesity in children is defined as having a Body Mass Index (BMI) greater than the 95th percentile for a child's age and sex.<sup>5</sup> In children, BMI for age and sex is an important tool in assessing weight status because, unlike adults, children's body compositions vary drastically by age and sex.<sup>5</sup> The increasing incidence of childhood obesity is largely attributed to three main factors – increased dietary intake, increased sedentary behaviors, and decreased physical activity – leading to a net positive energy balance.<sup>6</sup> Each of these factors was impacted by the COVID-19 pandemic.

The COVID-19 pandemic impacted dietary intake from both the perspective of an economic and a public health crisis. Food insecurity was most prevalent in communities of lower socioeconomic status.<sup>7</sup> Early in the pandemic, data revealed that those from families who lost jobs reported both the highest levels of food insecurity and the lowest engagement with food assistance programs.<sup>8</sup> While the Supplemental Nutrition Assistance Program (SNAP) expanded to support those through the pandemic, data suggest that it was only relevant to groups with higher levels of income stability and that it may not have impacted those most at risk for food insecurity.<sup>8</sup> From a public health perspective, closing schools helped mitigate the spread of COVID-19 early in the pandemic, however, it removed students from in-person classes where many reliably received nutritious meals through the federally funded National School Lunch Program (NSLP). An estimated 27 million to 78

million fewer lunches were served per week in March – November 2020 compared to the previous year.<sup>9</sup> In a study that compared NSLP participants from March to November 2020 to those in 2019, it was predicted that if an NSLP participant received no school meals in a week, they would increase caloric consumption by 640 calories and reduce overall consumption of calcium and vitamin D.<sup>9</sup> Further extrapolation of this prediction estimates an extra 3 billion to 10 billion additional calories per week were consumed by children, nationally, from March – November 2020 when compared to the previous year.<sup>9</sup>

Sedentary behaviors in children of all ages also increased during the COVID-19 pandemic. These sedentary behaviors are closely linked to screen time. Screen time increases were attributed both to the utilization of technology for education delivery and for recreation. Studies demonstrated that forced social distancing measures led to an increase in screen time by nearly 5 hours per week in the youngest students.<sup>10</sup> Another study further supports that elementary school students exhibited more sedentary behaviors and increased screen time; this led to adverse changes in sleep patterns and diet in this population.<sup>11</sup>

Physical activity across children of all grades decreased as a direct result of the COVID-19 pandemic. Both the amount of time allotted to physical activity and the intensity of physical activity decreased during the pandemic. Frequency and duration of organized physical activity was found to decrease with the implementation of social

distancing regulations in some countries.<sup>12</sup> One study revealed that young adults and students reported the greatest decline in self-reported physical activity during early phases of isolation.<sup>13</sup> There is some evidence which suggests physical education in the post-COVID era is of less intensity than what is typically recommended for children. The World Health Organization (WHO) recommends that children spend about 50% of their physical education class time engaging in moderate-to-vigorous physical activity (MVPA).<sup>14</sup> One study suggests that after the height of the COVID-19 pandemic, time spent in MVPA accounted for only 31-43% of a physical education class.<sup>14</sup> In short, both duration and intensity of physical activity performed by children decreased secondary to the COVID-19 pandemic.

One study from the Centers for Disease Control and Prevention (CDC) quantified the impact of increased caloric intake, increased sedentary behavior, and decreased physical activity on childhood obesity. The study consists of over 400,000 children from 2 to 19 years old, and it demonstrated that BMI doubled during the COVID-19 pandemic compared to pre-pandemic years.<sup>15</sup> It noted the most rapid increase in young school-age children who were overweight or obese pre-pandemic.<sup>15</sup> Moderately obese children gained about 5.5 pounds more than their expected gain while severely obese children gained about 5.8 pounds more than their expected gain over the course of nine months.<sup>15</sup> This demonstrates the culmination of physical health consequences the COVID-19 pandemic has had on childhood obesity.

## Endocrinopathies

In an already worsening childhood obesity epidemic in the United States, it is important to understand the trends in sedentary lifestyles during the COVID-19 pandemic and how they might play a role in future childhood obesity patterns. Besides the detriment to physical well-being caused by an overall positive energy balance, children also began to experience changes in endocrine function during the pandemic. Obesity is a known risk factor for COVID-19 susceptibility and risk of severe infection, partially secondary to the constant basal level of inflammation associated with obesity.<sup>16</sup> However, obesity may have also contributed to abnormal endocrine functioning in children during the pandemic. Globally, rates of endocrinopathies in children, specifically cases of precocious or rapidly progressive puberty and new-onset diabetes, have increased since 2019.<sup>17,18</sup> This section explores the connection between the COVID-19 pandemic and the rise of these endocrinopathies in children.

Although this trend in endocrine dysfunction does not necessarily result directly from children contracting SARS-CoV-2, the virus may have catalyzed subsequent endocrinopathy development in those who did. The connection between viral infection and disruption in endocrine physiology is complex, and effects often depend on which portion of the endocrine pathway is targeted by the virus.<sup>19</sup> Viruses typically evoke an immune pathway response in the host.<sup>19</sup> In the context of the endocrine system, this may result from damage to specific endocrine cells

through viral infection or replication, damage to the organ via direct inflammation or systemic immune response, or even alteration of hormonal response due to disruption by viral gene products or activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis.<sup>19</sup>

SARS-CoV-2 binds angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) on host cells in various organs throughout the body, including endocrine organs such as the hypothalamus, pancreas, thyroid, and gonads among others.<sup>20</sup> A poignant and well-studied example arising from the COVID-19 pandemic is the relationship between SARS-CoV-2 and diabetes mellitus. While diabetes was noted as a comorbidity that increased the risk of poorer outcomes early in the pandemic, COVID-19 infection became subsequently correlated with new-onset diabetes mellitus in certain patients.<sup>20</sup> Because pancreatic islet beta cells express high levels of ACE-2, SARS-CoV-2 can directly bind to and disrupt beta cell functioning. This leads to the activation of inflammatory cytokines and cell death, resulting in decreased insulin secretion, worsened glucose homeostasis, and, ultimately, the potential of diabetes.<sup>20</sup> Since the pandemic began, there has been an increase in both new diagnoses of Type 1 diabetes in children and severe diabetic ketoacidosis (DKA) as the first presentation of Type 1 diabetes.<sup>18</sup> This trend, identified in children and adults, demonstrates the interplay between viruses and their effect on endocrine pathophysiology.

Beyond the implications of viral infection on endocrinopathy development, the rise in obesity itself may have also contributed to endocrinopathy. In the pre-pandemic era, obesity was already considered a risk factor for Type 2 diabetes due to the associated insulin resistance.<sup>21</sup> During the pandemic, along with rising childhood obesity, studies have shown an increase in the incidence of Type 2 diabetes. Specifically, studies conducted in large pediatric hospitals in Alabama, Indiana, and California found that the number of new diagnoses of Type 2 diabetes were significantly higher in their respective institutions during the pandemic versus the pre-pandemic era.<sup>22</sup> Given the physiological interplay between obesity and Type 2 diabetes, this trend represents an area of further study.

Another interesting phenomenon noted during the pandemic was an increase in the cases of central precocious puberty and rapidly progressive puberty. Since the 1970s, the rise in childhood obesity has been linked to earlier onset of menarche and puberty young girls, with excessive BMI correlating to pubertal development as young as eight years of age.<sup>23</sup> Various mechanisms have been suggested for the correlation between obesity and earlier pubertal age. The neuroendocrine mechanism suggests that because leptin acts indirectly on gonadotropin-releasing hormone to permit puberty initiation and progression, the elevated leptin levels associated with obesity may jumpstart early pubertal development.<sup>23</sup> Other mechanisms suggest that androgen aromatization and decreased sex steroid

availability also contribute to early puberty in females.<sup>23</sup> Independent studies conducted in centers located in Italy, Turkey, Brazil, and China discovered significant increases in cases of central precocious puberty and rapidly progressive puberty during the pandemic - as high as 3x pre-pandemic numbers in certain countries- as compared to before.<sup>24,16,25</sup>

Hypotheses link this trend to an overall increase in BMI, through the aforementioned mechanisms, and possibly as resulting directly from contracting the virus via viral impact on hypothalamic cells.<sup>24</sup> Data on abnormal pubertal progression in boys is more limited as many of the studies focus on premature thelarche and menarche in females.

#### **Access to Healthcare**

Along with the increasing incidence of new diagnoses of endocrinopathies, children with chronic endocrine diagnoses appear to have been affected by the pandemic as well. A cross-sectional study of pediatric hospitals in southern Italy showed that from 2019 to 2020, the overall number of ED consultations decreased from pre-pandemic to during the pandemic, however, the number of urgent/emergent visits increased from 4.9% in March-May 2019, to 7.1% in March-May 2020.<sup>26</sup> Although this study was not specific to endocrine conditions, in general, it appears that as fear of the spread of SARS-CoV-2 grew, the willingness of families to receive healthcare for routine visits or even some more acute concerns lessened. This may have resulted in a more severe presentation of their conditions when medical attention was sought.

In concurrence with the aforementioned study, a systematic review conducted with multiple European and American studies discussing pediatric emergency department use during the pandemic found that all 25 articles included noted a decline in pediatric emergency departments visits.<sup>27</sup> Although this would correspond with a decline in visits for less acute health concerns, a potential consequence may be an increase in visits for medical emergencies, such as DKA, due to less frequent monitoring by healthcare professionals. According to a retrospective study across several pediatric emergency departments in Israel, there was an over 10% increase in DKA presentations in children with preexisting Type 1 diabetes in 2020 as compared to 2019.<sup>28</sup> Interestingly, a retrospective, multicenter study conducted in Saudi Arabia saw a dramatic increase in the cases of DKA with new-onset Type 1 diabetes, however, they also appreciated a decrease in DKA hospital admissions in children with established diabetes.<sup>29</sup> Even so, a worldwide study examining 22, 820 children involved in the SWEET (Better Control in Pediatric and Adolescent Diabetes: Working to Create Centers of Reference) project showed that although glycemic control was fairly maintained during the first wave of COVID, presentations of DKA in children with established Type 1 diabetes did increase by a significant margin in the countries with the highest mortality rates during the first wave.<sup>30</sup>

Data is limited when considering the impact of COVID on chronic endocrinopathies in children other than diabetes. Although SARS-CoV-2 may affect multiple endocrine organs,

at present, we were unable to find studies discussing decreased healthcare access or increased rates of severe presentations of other endocrinological emergencies (i.e. thyroid storm, adrenal crisis, etc) in children with chronic endocrinopathies.

### Healthcare Disparities

Healthcare disparities are defined as preventable differences in disease burden experienced by socially disadvantaged populations.<sup>31</sup> Disparities and inequities can be improved by addressing social determinants of health. It is important to understand which populations are at greatest risk of developing childhood obesity and endocrinopathies as well as which populations were most devastated by the COVID-19 pandemic to reveal the many forces impacting the development of these pathologies.

From a socioeconomic perspective, there is an increasing gap in childhood obesity between those of low and high socioeconomic status groups.<sup>32</sup> The rate of increasing childhood obesity is likely multifactorial, dually stemming from emotional and economic stress. Children of low socioeconomic status experience higher rates of stress, insecurity, depression, and anxiety.<sup>33</sup> One prospective study of over 9000 youth suggests these negative emotions- specifically depression- are associated with developing childhood obesity.<sup>34</sup> Another study specifically use hair cortisol levels as a biomarker for chronic stress; this study went on to suggest that children of lower socioeconomic status experience higher stress levels and activation of the HPA axis,

resulting in higher cortisol levels.<sup>35</sup> Consequences of these increased cortisol levels may include higher incidences of cardio metabolic disease in adulthood.<sup>35</sup> Of note, the financial hardship faced by children of low socioeconomic status also contributes to childhood obesity by reducing access to healthy lifestyle choices and promoting the consumption of more calorie-dense, unhealthy foods.<sup>36,37</sup>

There is also evidence to suggest that children from lower socioeconomic households are at an increased risk of diabetes. One study in Canada found that in households with children diagnosed with diabetes, food insecurity prevalence is dramatically increased compared to the general population of the country (21.9% compared to 9.2%).<sup>38</sup> Moreover, mean A1c levels in children from food-insecure households were higher than food-secure households.<sup>38</sup>

It is important to understand how disparities have affected the relationship between the consequences of the COVID-19 pandemic, obesity, and metabolic pathologies to care for children in the post-COVID era. It is evident that both pre-existing disparities and childhood obesity rates have increased during the pandemic.<sup>39</sup> The relationship between cardiometabolic conditions and socioeconomic status is bidirectional; as a consequence, increasing levels of childhood obesity will continue to enhance existing inequities and perpetuate poverty in vulnerable families.<sup>40,41</sup>

Some groups of children are susceptible to developing childhood obesity from what is

predicted to be a combination of both genetic and non-genetic factors.<sup>41</sup> Since the early 2010s, groups of children including Hispanic boys and non-Hispanic black girls have been developing obesity at higher rates than the general population.<sup>42</sup> In 2017, United States Preventative Services Task Force (USPSTF) put forth a statement describing the higher rates of obesity in Hispanic boys and African American girls; this statement clarified that the differences in obesity prevalence between these groups was likely multifactorial and attributed to both genetic and non-genetic factors.<sup>5</sup>

Children who are most at risk of developing obesity based on race/ethnicity are also at an increased risk of developing associated conditions including type 2 diabetes mellitus and polycystic ovary syndrome (PCOS).<sup>43,44</sup> Furthermore, Hispanic females with PCOS have demonstrated the most severe phenotype in studies with higher rates of hyperandrogenism and metabolic pathology.<sup>45</sup> Additionally, these youth are at an increased risk of undergoing precocious puberty.<sup>46,47</sup>

It is important to consider that children at risk of developing obesity and endocrinopathies secondary to healthcare disparities might have also faced unique challenges during the COVID-19 pandemic. For example, children from lower socioeconomic households faced food insecurity during the pandemic when they no longer received consistent school lunches. Moreover, children from disadvantaged backgrounds might not have had a safe space to engage in physical activity

with their physical education courses put on-hold during the era of virtual learning. The changes in diet and exercise regimen contribute to increased obesity and metabolic pathologies during the pandemic in populations which were already at greater risk.

### Conclusion

The relationship between the COVID-19 pandemic, childhood obesity, and endocrinopathies is complex. Measures taken to reduce the spread of SARS-CoV-2 had the adverse effect of exacerbating the already present childhood obesity epidemic. Along with a rise in childhood obesity, rates of endocrinopathies in children also rose, with prominent examples being diabetes mellitus and abnormal pubertal initiation. There is

evidence to suggest both direct influence of SARS-CoV-2 on this trend and indirect influence via the worsening of childhood obesity. In children with preexisting diabetes before the pandemic, evidence suggests an increase in DKA presentations during the pandemic, which may be related to decreased utilization of healthcare providers for less acute concerns. Children from disadvantaged backgrounds were at a higher risk of developing obesity and obesity-related comorbidities before the pandemic, and the COVID-19 pandemic may have further contributed to this phenomenon. Moving forward, additional research into the endocrine and metabolic effects of the pandemic will be necessary to elucidate how pervasive the pandemic has been in the growth and development of our children.

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