

COVID-19 Infection

BRIEF REVIEW

**Obstructive Sleep Apnea and COVID-19 Infection Comorbidity:
Analysis of the Problem in the Age Aspect**

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Abstract

In the literature, there are suggestions of a possible mutual influence between obstructive sleep apnea (OSA) and the novel coronavirus disease 2019 (COVID-19). The aim of this review is to analyze data found in the literature related to pathogenetic aspects of the impact of OSA on COVID-19, and vice versa, and features of the course of this comorbidity in both adulthood and childhood. Information was searched in MEDLINE, PubMed, EBSCO, and RSCI databases, which presented some data for the connection between COVID-19 and OSA, as well as aspects of OSA and COVID-19 comorbidity for adults and the elderly. The common pathophysiological pathways leading to increased systemic inflammation and adverse consequences of OSA and COVID-19 infection do coexist and were revealed in detail. We paid special attention to aspects of this comorbidity in children, and found that research in this area was lacking. Based on this information, it should be concluded that: 1) more pediatric studies of links between OSA and COVID-19 are urgently needed; 2) screening hospitalized COVID-19 patients with tools to detect OSA could identify those at risk for a severe course of these diseases and adverse outcomes; 3) treating OSA will allow increasing the likelihood of developing a robust and long-lasting post-COVID-19 adaptive immunity in these patients. (**International Journal of Biomedicine. 2020;10(4):312-315.**)

Key Words: obstructive sleep apnea • COVID-19 • comorbidity • pathogenesis • adults • children

Just over half a year has passed since the World Health Organization (WHO) declared the COVID-19 outbreak a public health emergency of international concern. At the time, there were only 100 cases outside of China and no deaths. Since then, the incidence has been increasing exponentially, affecting every country in the world. WHO data, published on August 16, 2020, reported 21,294,845 cases of COVID-19 worldwide, with 761,779 deaths, but on September 21, 2020, reported 30,949,804 cases in 235 countries, and 959,116 deaths.⁽¹⁾ The number of new cases of COVID-19 increases week by week and reaches 2,000,000 per week (Fig.1).⁽²⁾ In the Russian Federation as of September 21, 2020, the number of cases of COVID-19 infection was 1,109,595, with 6,196 deaths.⁽³⁾ The COVID-19 pandemic has placed an enormous burden on the global health care system

with numerous consequences. The secondary effects of this pandemic, along with major disruptions to essential health care services, are having a huge impact on politics, the economy, and people's daily lives.

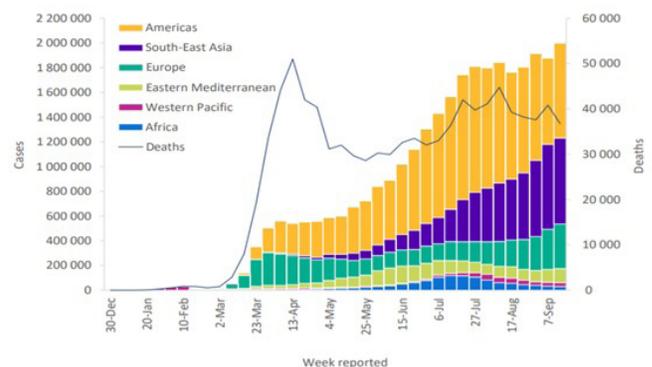


Fig. 1. Number of COVID-19 cases reported weekly by worldwide and global deaths, December 2019 through September 2020 (adapted from (2)).

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COVID-19 was predominantly more prevalent among adults and the elderly at the beginning of the outbreak, and the percentage of confirmed cases among children and adolescents was relatively small. The Chinese Novel Coronavirus Pneumonia Emergency Response Epidemiology Team reported that about 2% of 44,672 confirmed cases of COVID-19 in China through February 11, 2020, were children between 0 and 19 years of age;⁽⁴⁾ of these, 0.9% were subjects younger than 10 years old. One month later in Italy, Livingston et al. found that 1.2% of all confirmed cases (22,512) of COVID-19 were children, with no deaths.⁽⁵⁾ At the same time, of 4,226 COVID-19 cases detected in the United States, 5% were children.⁽⁶⁾ Importantly, more than 90% of ill children were asymptomatic or had mild or moderate symptoms of COVID-19 infection. Since then, the number of child COVID-19 cases has increased significantly, especially in younger age groups, and the disease increasingly began to manifest with so-called «pediatric multisystem inflammatory syndrome»⁽⁷⁾ with severe outcomes;⁽⁸⁾ therefore, high attention and care should be directed to children and adolescents with COVID-19, just like adult patients. It was shown that COVID-19 is an acute, self-limiting disease, but some patients can die, according to Xu's et al. reported mortality rate of 2% in adults.⁽⁹⁾ The Centers for Disease Control and Prevention (CDC) has published data of deaths involving COVID-19 with a focus on ages 0-18 years in the United States, and on August 26, 2020, reported that in the US there were 29 deaths among children aged 0-4 and 65 among those aged 5-18 years.⁽¹⁰⁾

Some studies have reported a higher COVID-19 incidence in men than in women (0.31/100,000 vs 0.27/100,000, respectively).⁽¹¹⁾ Wherein, the case mortality rate for males was also higher than for females (2.8% vs 1.7%, respectively), with a similar trend in children and adolescents, reported by the CDC in the US.⁽¹⁰⁾ It has also been proven that the risk of infection and complications increases significantly in the presence of comorbidities (both adults and children): Patients who reported no comorbid diseases had lower mortality rates than those with comorbid conditions, such as cardiovascular diseases, diabetes, chronic obstructive pulmonary disease, or cancer.^(4,12)

All of the above-mentioned prompted us to closely study the features of the pathogenetic mechanisms and relationships between COVID-19 and one comorbidity, namely OSA, that is very important for the health care of both adults and children. It should be noted that, despite the obvious relevance and severity of this problem worldwide and numerous discussions in the foreign literature, there are many works of Russian scientists about COVID-19 infection and coexisting diseases in adults,^(13,14) while only one publication is devoted to the association between COVID-19 and OSA.⁽¹⁵⁾ But there are no Russian publications, and just a single foreign one, on this problem in pediatric patients.

The aim of this review is to analyze data found in the literature related to pathogenetic aspects of the impact of OSA on COVID-19, and vice versa, and features of the course of this comorbidity in both adulthood and childhood.

Information was searched in MEDLINE, PubMed, EBSCO, and RSCI databases.

OSA and COVID-19 infection in adults and the elderly

By definition, OSA is a condition characterized by

recurrent episodes of upper airway obstruction during sleep, due to anatomical narrowing of the airway, arousals, and recurrent nocturnal intermittent hypoxemia.⁽¹⁶⁾ OSA is common and the incidence is increasing worldwide. Interestingly, the rate of the condition has a gender dimorphism, as in COVID-19. It is estimated that OSA affects 27% of men and 11% of women in the middle-aged adult population.⁽¹⁷⁾ This disease is significantly underdiagnosed, due to lack of awareness and its insidious course, and often remains untreated.

OSA is strongly associated with COVID-19 comorbidities, namely cardiovascular disease, hypertension, diabetes, and obesity.⁽¹⁸⁾ Studies published from April to September 2020, worldwide, on adult and elderly subjects highlighted the strong overlap between OSA and the risk factors for adverse outcomes of COVID-19 infection.⁽¹⁹⁻²⁷⁾ It is known that, both in patients with OSA and COVID-19 infection, there are associations with increased systemic concentrations of IL-6, IL-17, TNF- α and other pro-inflammatory mediators (e.g., «cytokine storm»)^(28,29) as well as oxidative stress (inevitably accompanying OSA and coexisting diseases),^(30,31) which confirms the possibility of potentiating systemic inflammation in the case of their comorbidity and acts as a major determinant of the adverse consequences of these coexisting diseases (Fig.2). Suen et al. has reported that OSA can potentially aggravate inflammation in COVID-19-related sepsis or acute respiratory distress syndrome.⁽³²⁾ The CORONADO study showed highly significant associations between OSA and the risk of death on day 7 of COVID-19 disease (adjusted OR 2.65).⁽³³⁾ Cade et al. also described OSA as a risk factor for COVID-19 mortality and severe morbidity, highlighting the need for close monitoring of patients with OSA who become infected.⁽³⁴⁾

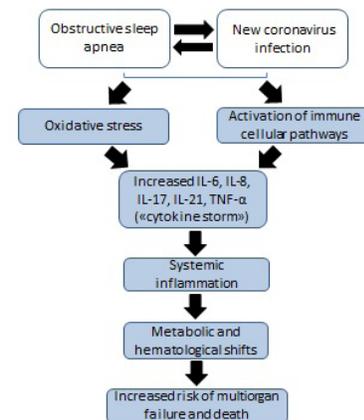


Fig. 2. The common schema illustrating of a cascade of pathophysiological pathways that result in increased systemic inflammation and adverse consequences if obstructive sleep apnea and COVID-19 infection are comorbidity.

There are suggestions of possible links of mutual influence of OSA and COVID-19. OSA could be also added to the severity of the pulmonary inflammatory process of COVID-19 infection. An increased incidence of OSA in COVID-19 patients through the dysregulation of the renin-angiotensin system and hypertension,⁽³⁵⁾ as well as hyperinflammatory response,⁽³²⁾ which can occur in COVID-19 pneumonia, can

cause multiorgan failure.⁽³⁶⁾ Furthermore, management of OSA patients with COVID-19 infection requires special care and precautions.^(37,38)

Children's aspects of OSA and COVID-19 comorbidity

It is well known that OSA affects 1%-5% of all children and adolescents⁽³⁹⁾ and is associated with COVID-19 comorbidities (e.g. hypertension and obesity), as in adults and the elderly,⁽⁴⁰⁻⁴²⁾ which along with the appearance of COVID-19-induced lung injury in children and an almost equal OSA and COVID-19 incidence in the pediatric population, is a serious problem for children's healthcare services. Despite increasing evidence showing children have more mild presentations and better outcomes with COVID-19, there is very limited documentation in the medical literature of apnea cases, especially coexisting OSA, potentially aggravating the course of the disease. It has been reported that sleep-disordered breathing in children and adolescents with COVID-19 may manifest by episodes of apnea. In three studies, Needleman et al.,⁽⁴³⁾ Brabin et al.,⁽⁴⁴⁾ and Enner et al.⁽⁴⁵⁾ described COVID-19-associated apnea and circumorally cyanosis in a 3-week-old, full-term male infant; and neonatal apnea as initial manifestation of COVID-19 infection (a type of apnea was not marked: central or obstructive in both cases), and COVID-19-associated encephalopathy characterized by focal seizures and central apnea in a 14-year-old girl. We found information about a 3-year-old boy with Down syndrome and many comorbidities, including OSA, with dependence on continuous positive airway pressure (CPAP), who was infected by COVID-19, prompting development of mild hypotension and the need for an increase in CPAP.⁽⁴⁶⁾ Today, this is perhaps the only finding about a case of COVID-19 infection in a pediatric patient with OSA as a chronic lung disease.

Conclusion and outlook

Based on our analysis, it can be concluded that such a serious problem as COVID-19 infection against the background of coexisting diseases, namely chronic respiratory pathology, for example OSA, in adult and elderly patients is being carefully studied and widely discussed by scientists from many countries. However, there are few studies in the pediatric population are single, which urgently necessitates research into links between OSA and COVID-19 in childhood and adolescence. It should also be remembered that screening hospitalized COVID-19 patients with tools to detect OSA (subjective or/and objective, such as polysomnography) could identify those at risk for adverse outcomes, and by subsequently restoring adequate sleep, we can not only reduce the incidence of complications in such patients but also increase the likelihood of developing a robust and long-lasting post-COVID-19 adaptive immunity.

Competing Interests

The authors declare that they have no competing interests.

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