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Clinical practice guideline: Approach to childhood asthma in the era of COVID-19: The official statement endorsed by the Saudi Pediatric Pulmonology Association (SPPA)

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Key words: Asthma, COVID-19, Saudi Pediatric Pulmonology Association (SPPA)
Abstract

Coronaviruses are a large family of viruses that can infect humans, which may result in mild symptoms similar to those of the common cold. COVID-19 is most recent subtype similar or even worse than the two previous pandemic strains which were the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV). The first cases of COVID-19 emerged in December 2019. Since then, the virus causing the disease has infected more than four million around the globe and led to death of hundreds of thousands of people. We think addressing the management of asthma in the era of this pandemic is important for the several reasons: high prevalence of asthma in Saudi Arabia, further, majorities were uncontrolled disease. The statement will provide special instructions and answers to common questions of physicians dealing with asthmatic children during this pandemic.
1. Introduction

Coronaviruses are a large family of viruses that can infect humans as well as other mammals. There are seven strains that infect humans. The common and fortunately less serious strains are HCoV-OC43, HCoV-HKU1, HCoV-229E and HCoV-NL63. Infections with these viruses usually result in mild symptoms similar to those of the common cold. However, infections with the three other strains lead to more severe diseases; they are MERS-CoV, SARS-CoV and the recently discovered SARS-CoV-2, which is mostly known by the disease it causes, COVID-19.\textsuperscript{1,2} The first cases of COVID-19 emerged in December 2019. Since then, the virus causing the disease has infected millions around the globe and led to death of hundreds of thousands of people.\textsuperscript{3} In Saudi Arabia, the first case of COVID-19 was confirmed on March 2\textsuperscript{nd}. Since then, the disease has been curbed (with strict intervention), and the cases are not overwhelming the healthcare facilities.\textsuperscript{4} For unknown reasons thus far, COVID-19 is mainly affecting adults more than children.\textsuperscript{5} In an article from China, it was reported that 2.1\% of all confirmed cases were children less than 19 years of age. Similarly, in Italy, the incidence was approximately 1.4 \%.\textsuperscript{6} While no children younger than 19 died in Italy, one child died in China.\textsuperscript{7}
We think addressing the management of asthma in the era of this pandemic is important for the following reasons:

1) The prevalence of asthma in Saudi Arabia is high, and it is increasing; in some recent reports, the prevalence was reported to be greater than 20%.\textsuperscript{8}

2) Asthma in Saudi Arabia is often not well controlled. The status of being uncontrolled ranged from 45% up to 64%\textsuperscript{9,10}

3) COVID-19 presentation has many similarities to the typical asthma exacerbations, and it will be difficult to differentiate between them.\textsuperscript{5}

4) The social distancing and quarantine practices are unprecedented in recent history. Many recent reports have described evidence of significant mental strain, such as anxiety, fears and depression. These factors may affect asthma control both directly and indirectly.\textsuperscript{11,12}

2. **The Objective of this statement is to provide** special instructions and answers to common questions of physicians dealing with asthmatic children during this pandemic.

3. **Method:**

We searched PubMed up to May 2020 using the following words in different combinations: asthma, exacerbation, COVID-19, inhalation, nebulizer, and steroid. Search filter include publications in the last 2 years, human species, and age less than 18 years. With these searches 30 were identified. All were included. Few Guidelines were published for this was intensively reviewed. We understood
common the Pandemic COVID-19 and does it affect modalities of treatment of asthma or asthma exacerbation. The evidence was inspired from the recommendations in the center of evidence-based medicine website (www.cebm.net), listed by Burns et al.13

4. Concern during the pandemic

There are many concerns were raised by both parents and health care providers in how to treat asthma during the pandemic, the following are the main concerns:

4.1. Do children with asthma have a higher risk to be infected with COVID-19?

The answer so far is no. In a series of severe COVID-19 adult cases in Wuhan, 0.9% had asthma, while the population prevalence of asthma was 6.4%. (14) In another nationwide study in China, they found that 25% of 1590 admitted patients had comorbidities, and none of them had asthma.15

4.2. What are the objectives of management of asthma patients during the COVID-19 pandemic?

There are no substantial differences from the usual guidelines. The hallmark of “control” remains the same, with the objective of treating with minimal medication, utilizing a step up, step down approach.16 However, the current COVID-19 pandemic made access to care more challenging. We advise that patients be kept on the minimal amount of controller therapy and to avoid withholding the controller therapy. It is imperative to reiterate that the situation is
evolving and that more data will emerge overtime. Furthermore, families should be educated about the chronic nature of asthma and the importance of adherence. The techniques of the recommended device(s) should be reviewed. Families should also be advised to check their medication supply.

A Written Action Plan (WAP) is a prescription that helps patients and their caregivers to use the medications based on patients’ symptoms. Such a plan was found to decrease asthma exacerbations and to result in better adherence to medications. We highly suggest using a WAP during this pandemic. The general public recommendations during this pandemic should be followed. Social distancing and hand hygiene should be practiced. The curfew and staying home may expose children to passive smoking; addressing the latter with caregivers is warranted.

4.3. What are the differences between common cold, influenza and COVID-19?

Viral illnesses are the most common trigger of asthma in children. These common respiratory infections can be very difficult to differentiate from COVID-19. They all affect the respiratory tract, and they have similar symptoms, especially in the first stages.

While seasonal flu and COVID-19 give you respiratory symptoms as well as gastrointestinal (GI) symptoms, common colds will rarely result in diarrhea or other GI symptoms. Fever is a common symptom of all infections. However, fever was a main manifestation of COVID-19, and interestingly, higher and more
persistent fevers were noticed in severe cases.\textsuperscript{20,21} Other symptoms such as anosmia, shortness of breath, chest pain, headache, fatigue, skin rash, and red eyes, among others, were reported.\textsuperscript{22,23} Furthermore, the timelines of these symptoms vary, and thus far, they are unpredictable. As an example, some patients will not have a fever for few days while they have only runny nose.\textsuperscript{23} In a series of eight severe pediatric cases, tachypnea was found in all patients, while fever and cough were found in only six patients.\textsuperscript{24}

4.4. Shall we continue using inhaled corticosteroids?

Inhaled corticosteroids (ICS) are the main controller therapy and are superior to all other anti-inflammatory controller therapies.\textsuperscript{25} However, there have been some concerns about the possible hazardous effect of systemic steroids on patients with COVID-19.\textsuperscript{26} These concerns were mainly based on observations during the 2003 SARS outbreak, which led to some debates in the medical community about the use of steroids in patients with COVID-19. However, many recent studies, especially concerning critically sick patients, are supportive of the cautious use of systemic steroids.\textsuperscript{27} Obviously, these concerns are projected toward the systemic, and not the inhalational, use of steroids. We think that the benefits of ICS controlling asthma outweigh the theoretical risks. Therefore, we highly suggest continual use of ICS as the mainstay controller therapy. Furthermore, allergic rhinitis is a common comorbidity of asthma. The European Academy of Allergy and Clinical Immunology (EAACI) recommend continued use of nasal steroids for patients with allergic rhinitis (AR).\textsuperscript{28}
4.5. **What about oral steroids?**

The use of oral steroids as a maintenance therapy is very rare in children, and such patients are followed by an asthma specialist. However, short courses of steroids are frequently used as a rescue therapy in asthma exacerbation. The apparent risk with steroids is far less than the benefits of aborting an exacerbation. Therefore, we suggest continuing the practice of prescribing short course of steroids if clinically indicated. We suggest prescribing the lower range of the dose (0.5 mg to 1 mg per kilogram per day, prednisolone equivalent).

4.6. **Can asthma patients continue using nebulization?**

Nebulization is a process where a liquid is transformed into small liquid droplets suspended in air, or what is called aerosol. The virus can remain suspended in air for up to two hours, which carries the risk of transmitting pathogens to others. However, this observation was performed in a research lab and was not replicated in real life.

Almost all asthma guidelines recommend using metered dose inhalers (MDIs) with a valved holding chamber (VHC) or dry powder inhalers rather than nebulization. Therefore, following such guidelines during this pandemic seems logical and potentially safer. We suggest avoiding the use of nebulization at homes. If the alternative is not feasible, cautious use in a private area and never sharing the machine with others are advised.
On the other hand, almost all health institutions across the country use nebulization as the mode of aerosolizing medications. For the past few years, many institutions around the world have adopted using MDIs with VHCs instead of nebulization.\textsuperscript{32} This is based on the fact that the two inhalation techniques yield similar clinical scores and outcomes.\textsuperscript{33}

Therefore, we suggest using MDIs with the appropriate VHCs instead of nebulization in health institutions. This is of particular importance in the settings of acute care where the possibility of viral cross-infections is high. Obviously, the VHC should not be shared. Of course, some exceptions will arise, such as severe asthma exacerbation, uncooperative patients or those with decreased levels of consciousness. If nebulization is carried out, appropriate isolation should be maintained, and healthcare providers should wear the recommended personal protective equipment (PPE). The Saudi Initiative for Asthma (SINA) in collaboration with The Saudi Thoracic Society (STS) and its subsidiary Saudi Pediatric Pulmonology Association (SPPA) have released a national statement on asthma management of adult and children during the COVID-19 pandemic that includes preferencing the use of MDIs with the appropriate VHCs instead of nebulization.

The Saudi Initiative for Asthma\textsuperscript{16, 34} and The British Thoracic Society\textsuperscript{35} recommend the following doses:

Less than 20 kg: 4-6 puffs of salbutamol MDI are equivalent to 2.5 mg of nebulized salbutamol
More than 20 kg: 10-12 puffs of salbutamol MDI are equivalent of 5 mg of nebulized salbutamol.

4.7. What about follow up?
As the current COVID-19 pandemic limited the access to routine outpatient visits to asthma clinics, alternative ways of remote follow up is recommended. Virtual clinic, phone calls, and other means of telemedicine should be utilized to maintain continuity of care for asthmatic patients. Access to medications should be ensured utilizing “mail-order” prescriptions.

4.8. What about pulmonary function tests (PFTs)?
Spirometry or other forms of PFTs may potentially increase the risk of COVID-19 transmission and should be avoided as much as possible.36

5. Conclusion:
The current pandemic of COVID-19 in children is often mild and self-limited disease,37 but, it the pandemic have changed many medical practice for both patients and health care providers, among such is asthma where, nebulization should be restricted due to the concern on aerosolization of corona virus and spread of the infection for this reason, should be avoided in the emergency setup.38 The prophylaxis should continue as planned, Asthma action plan should be provided, MDI and spacer in the preferred way for bronchodilator and spirometry should be avoided.

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Abbreviations

COVID-19: Coronavirus. Novel Coronavirus-2019.
MDI: Metered dose inhaler
VHC: Valved holding chamber
PPE: Personal protective equipment
WAP: Written Action Plan
SINA: The Saudi Initiative for Asthma
STS: The Saudi Thoracic Society
SPPA: Saudi Pediatric Pulmonology Association

References:

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020 Feb 15;395(10223):497-506.

2. Gaunt ER, Hardie A, Claas ECJ, Simmonds P, Templeton KE. Epidemiology and Clinical Presentations of the Four Human Coronaviruses 229E, HKU1, NL63, and OC43 Detected over 3 Years Using a Novel Multiplex Real-Time PCR Method. J Clin Microbiol. 2010; 48(8): 2940–2947.

3. Recovered from https://www.worldometers.info/coronavirus

4. Recovered from https://www.worldometers.info/coronavirus/country/saudi-arabia

5. Wu Z, Mcgoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a
Report of 72,314 Cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020; 323(13):1239-42.

6. De Natale G, Ricciardi V, De Luca G, De Natale D, Di Meglio G, Ferragamo A, et al. The COVID-19 infection in Italy: a statistical study of an abnormally severe disease. Journal of Clinical Medicine. 2020 May;9(5):1564.

7. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics. 2020 Mar 1.

8. Alahmadi TS, Banjari MA, Alharbi AS. The prevalence of childhood asthma in Saudi Arabia. Int J Pediatr Adolesc Med. 2019; 6(2):74-77.

9. Al-jahdali HH, Al-hajjaj MS, Alanezi MO, Zeitoni MO, Al-tasan TH. Asthma control assessment using asthma control test among patients attending 5 tertiary care hospitals in Saudi Arabia. Saudi Med J. 2008; 29(5):714-7.

10. Alsahn B, Alshamrani A, Alzahrani A, Alsahmi O, Alqudhybi A. Asthma Control Assessment Using Asthma Control Test Among Pediatric Patients Attending a Tertiary Care Hospital in Saudi Arabia. Egyptian Journal of Hospital Medicine. 2017; 68 (2): 1215-1223.

11. Vazquez K, Sandler J, Interian A, Feldman JM. Emotionally triggered asthma and its relationship to panic disorder, ataques de nervios, and asthma-related death of a loved one in Latino adults. J Psychosom Res. 2017; 93:76-82.
12. Weiser EB. The Prevalence of Anxiety Disorders among Adults with Asthma: A Meta-Analytic Review. J Clin Psychol Med Settings. 2007; 14: 297–307.

13. Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. Plast Reconstr Surg 2011; 128:305-10.

14. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. Journal of Allergy and Clinical Immunology. 2020 Apr 12.

15. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. European Respiratory Journal. 2020 May 1;55(5).

16. Al-Moamary MS, Alhaider SA, Alangari AA, Al Ghobain MO, Zeitouni MO, Idrees MM, et al. The Saudi Initiative for Asthma-2019 Update: Guidelines for the diagnosis and management of asthma in adults and children. Annals of thoracic medicine. 2019 Jan;14(1):3.

17. Macgillivray ME, Flavin MP. Canadian paediatric asthma action plans and their correlation with current consensus guidelines. Paediatr Child Health. 2014; 19(7):362-6.

18. Ducharme FM, Zemek RL, Chalut D, McGillivray D, Noya FJ, Resendes S, et al. Written action plan in pediatric emergency room improves asthma prescribing, adherence, and control. American journal of respiratory and critical care medicine. 2011 Jan 15;183(2):195-203.
19. Ring N, Jepson R, Pinnock H, Wilson C, Hoskins G, Wyke S, et al. Developing novel evidence-based interventions to promote asthma action plan use: a cross-study synthesis of evidence from randomised controlled trials and qualitative studies. Trials. 2012 Dec;13(1):216.

20. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine. 2020 Apr 30;382(18):1708-20.

21. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. bmj. 2020 Feb 19;368.

22. Michelen M, Jones N, Stavropoulou C. In patients of COVID-19, what are the symptoms and clinical features of mild and moderate cases. Centre for Evidence-Based Medicine https://www.cebm.net/covid-19/in-patients-of-covid-19-what-are-the-symptoms-and-clinical-features-of-mild-andmoderatecase/accessed. 2020 Apr;16.

23. Heidari F, Karimi E, Firouzifar M, Khamushian P, Ansari R, Ardehali MM, et al. Anosmia as a prominent symptom of COVID-19 infection. Rhinology. 2020 Apr 22;58(3):302-3.

24. Sun D, Li H, Lu XX, Xiao H, Ren J, Zhang FR, et al. Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center’s observational study. World Journal of Pediatrics. 2020 Mar 19;1-9.
25. Van aalderen WM, Sprikelman AB. Inhaled corticosteroids in childhood asthma: the story continues. Eur J Pediatr. 2011; 170(6):709-18.

26. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA internal medicine. 2020 Mar 13.

27. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive care medicine. 2020 Mar 28:1-34.

28. Bousquet J, Akdis C, Jutel M, Bachert C, Klimek L, Agache I, et al. Intranasal corticosteroids in allergic rhinitis in COVID-19 infected patients: An ARIA-EAACI statement. Allergy. 2020 Mar 31.

29. Ari A, De andrade AD, Sheard M, Alhamad B, Fink JB. Performance Comparisons of Jet and Mesh Nebulizers Using Different Interfaces in Simulated Spontaneously Breathing Adults and Children. J Aerosol Med Pulm Drug Deliv. 2015; 28(4):281-9.

30. Tang JW, Li Y, Eames I, Chan PK, Ridgway GL. Factors involved in the aerosol transmission of infection and control of ventilation in healthcare premises. J Hosp Infect. 2006; 64(2):100-14.

31. The Global Initiative for Asthma (GINA) 2020 main report. Available at https://ginasthma.org/gina-reports/
32. Alhaider SA, Alshehri HA, Al-Eid K; Replacing nebulizers by MDI-spacers for bronchodilator and inhaled corticosteroid administration: Impact on the utilization of hospital resources; Int J Pediatr Adolesc Med. 2014 Sep; 1(1):26-30.

33. Roncada C, Andrade J, Bischoff LC, Pitrez PM. Comparison of Two Inhalational Techniques for Bronchodilator Administration in Children and Adolescents with Acute Asthma Crisis: A Meta-Analysis. Rev Paul Pediatr. 2018; 36(3):364-371.

34. The Saudi Initiative for Asthma (SINA) advices on asthma management of adult and children during the COVID-19 pandemic; https://saudithoracicsociety.org/

35. https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-advice-for-healthcare-professionals-treating-patients-with-asthma/

36. Rasam SA, Apte KK, Salvi SS. Infection control in the pulmonary function test laboratory. Lung India: official organ of Indian Chest Society. 2015 Jul;32(4):359.

37. Al-Hajjar S, McIntosh K. Pediatric COVID-19: An Update on the Expanding Pandemic. International Journal of Pediatrics & Adolescent Medicine. 2020 May 18.
38. Levin M, Morais-Almeida M, Ansotegui IJ, Bernstein J, Chang YS, Chikhladze M, et al. Acute asthma management during SARS-CoV2-pandemic 2020. World Allergy Organization Journal. 2020 May 14:100125.