The effects of the COVID-19 lockdown on severe asthma in patients taking biologic therapy and air pollution in Riyadh

**Khan Mohammad Ayaz[1,2,3], Rajendram Rajkumar[1,2,4], Al-Ghamdi Basma[3],
Al-Jahdaly Emad[5], AL-Harbi Abdullah[1,2,3], Hayyan Hajar[1,2,3],
Obaidi Mostafa Mohammad[1,4], Hamdan AL-Jahdali[1,2,3]**

[1]Department of Medicine, College of Medicine, King Saud University for Health Sciences, [2]King Abdullah International Medical Research Centre, [3]Department of Medicine, Pulmonary Division, Ministry of National Guard-Health Affairs, [4]Department of Medicine, Internal Medicine Division, Ministry of National Guard-Health Affairs, Riyadh, [5]Department of Occupational and Environmental Medicine, College of Medicine, Umm AlQura University, Makkah, Saudi Arabia

Address for correspondence:
Dr. Hamdan Al-Jahdali, McGill University. King Saud University for Health Sciences, Riyadh, Saudi Arabia.Pulmonary Division, Sleep Disorders Center, King Abdulaziz Medical City, Riyadh, Saudi Arabia. E-mail: Jahdalih@gmail.com

Abstract:

BACKGROUND: The curfews and lockdowns imposed during the COVID-19 pandemic may decreased the volume of traffic and reduced air pollution. In addition, social distancing measures may contribute to reducing infection and asthma exacerbation.

OBJECTIVE: The objective of this study was to assess asthma control and asthma medication use among severe asthmatics on biologics before and after the COVID-19 pandemic.

METHODS: This is a cross-sectional survey study of patients with severe asthma receiving biologic therapy at King Abdulaziz Medical City-Riyadh, Saudi Arabia. We looked at the effects of the COVID-19 lockdown on this cohort of severe asthmatics on biologic therapy from March till June 2020 over a period of 12 weeks. We investigated changes in patients' symptoms and asthma control using the asthma control test (ACT) score and other parameters including emergency department visits, hospitalizations, use of oral prednisolone, changes in inhaler therapy, frequency of bronchodilator use, and patient perception of their symptoms before and after the lockdown period.

RESULTS: A total of 56, Female 39 (69%), mean age ± SD 47.4 ± 13.8 years. The duration of bronchial asthma since diagnosis ranged from 4 to 30 years. Most patients had been treated with omalizumab (47, 84%); the rest received mepolizumab (7, 12.5%) and dupilumab (2, 3.6%). All these patients had been on biologic therapy for 5 months, ranging from 5 to 120 months. Most of the patients (45, 80.4%) agreed that their symptoms of asthma had improved with biologic therapy. Most of the patients felt that overall asthma symptoms are better after curfew and lockdown 28 (50%). Less use of bronchodilators postcurfew was reported in 38% of the patients. Asthma control (≥20) using ACT score was significantly higher among patients in postcurfew and lockdown period compared to precurfew period 34 (61.7%) and 23 (41%) (*P* = 0.001), respectively.

CONCLUSIONS: Asthma control was better postcurfew and lockdown. A decrease in air pollution and social distances may be a contributing factor.

Keywords:

Biologics, COVID-19, severe asthma

Asthma is a chronic inflammatory condition of the airways that results in variable bronchial hyperresponsiveness and airflow limitations causing symptoms.[1] Recent data suggest that around 650 million people live with some degree of asthma symptoms worldwide.[2] Hospitalization and medications are the most important associated direct costs, while work and school absenteeism account for the greatest percentage of indirect costs.[3,4]

During coronavirus disease 2019 (COVID 19 the world re evaluated every aspect of contemporary life taken for granted in 2019; nevertheless, an expected increase

in exacerbations and death due to asthma did not materialize.[5]

The curfews and lockdowns imposed during the COVID-19 pandemic may have prevented transmission of other infections besides severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Furthermore, the decreased volume of traffic and social distancing measures (social distance may contribute to reducing infection but not air pollution) are likely to have reduced air pollution.

Air pollution from ozone (O_3), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and particulate matter (PM) may induce or aggravate asthma.[6] According to a number of published meta-analyses,[7,8] these atmospheric pollutants are associated with higher incidence, prevalence, or worsening of symptoms of asthma and increase hospitalizations. Regarding the short-term effects of air pollutants in terms of exacerbations or worsening of symptoms, three studies have found an association with PM, NO_2, SO_2, carbon monoxide (CO), and O_3.[9] The main pollutant found in traffic and vehicle emissions is NO_2.

Hence, enforced social distancing and "shielding" of patients with chronic respiratory disease may have improved symptoms in patients with asthma. However, emerging data on the risk of COVID-19 to people with asthma are inconsistent. Early reports suggested that asthma is not a risk factor for more severe infection with SARS-CoV-2.[10] The prevalence of asthma in two cohorts of patients with COVID-19 in Wuhan, China, was 0%–0.9%. Similar statistics were reported in study populations from other countries.[10] Omalizumab (an anti-immunoglobulin [Ig] E antibody used in the treatment of severe asthma) may protect against the development of worse COVID-19. Omalizumab enhances antiviral immunity via a downregulation of the high-affinity IgE receptor on plasmacytoid dendritic cells.[11,12]

Thus, asthma and treatment with biologic agents (e.g., omalizumab) may prevent infection with SARS-CoV-2 and reduce the severity of COVID-19. Indeed, many countries reported that hospitalizations due to asthma actually dropped substantially during the pandemic.[13] It is not clear whether the decrease was due to a reduction in symptoms or reluctance to visit hospitals. Lockdown with social distancing was the major measure to mitigate cross infection and spread of COVID-19.[14,15]

The aim of this study was therefore to determine the impact of the COVID-19 pandemic lockdown and enforced social distancing measures on patients with severe asthma treated with biologic agents.

Methods

Study design
This is a cross-sectional survey study of patients with severe asthma receiving biologic therapy at King Abdulaziz Medical City-Riyadh (KAMC-R), Saudi Arabia. This is a 1600-bed tertiary care university hospital. The division of pulmonology has subspecialty clinics including severe asthma clinics. We looked at the effects of the COVID-19 lockdown on this cohort of asthmatics on biologic therapy from March till June 2020 over a period of 12 weeks in Riyadh, Saudi Arabia.

Data on levels of air pollution in Riyadh over this period were provided by the Saudi Meteorological Office. The lockdown and social distancing rules led to a significant reduction in air pollution due to reduced traffic and industrial activities in and around Riyadh.

The study cohort includes all severe asthmatics who are on biologics in KAMC-R.

The frequency of treatment administration is as per the standard manufacturer's recommendation and Food and Drug Administration approval dosage for various biologic agents. Treatment is administered on site at KAMC by specialist nurses.

We investigated changes in patients' symptoms and asthma control (asthma control test [ACT] is not about life quality) using the ACT score after the lockdown and other parameters including emergency department (ED) visits, hospitalizations, use of oral prednisolone, changes in inhaler therapy, deaths, and patient perception of their symptoms in lockdown period.

Ethical approval
The Institutional Review Board (IRB) of KAMC at the King Abdullah International Medical Research Center, Riyadh, Saudi Arabia, approved this study.

Sample size estimation
Based on the total number of severe asthma patients registered with the clinic (60), assuming response distribution of 50%, the estimated sample size required to obtain 5% margin of error at 95% level of confidence, was 53. To allow for refusal to participate, all patients registered to attend the severe asthma clinic at KAMC were invited. Only those who consented to the survey were included.

Survey development
The data collection sheet for the telephone survey was reviewed by three consultants who defined and agreed the information required for the survey. The survey had six sections.

The first section collected standard demographic data. The second section was about asthma history and the use of biologic therapy. The third section asked about patients' usual maintenance therapy for asthma before the pandemic, and during social distancing enforcement at the time of the COVID 19 pandemic. The fourth section was about the effect of the COVID-19 pandemic and social distancing on the management of asthma. The fifth section was about need for emergency treatment for asthma during the COVID-19 pandemic and the period of enforced social distancing. This included bronchodilator use, use of oral steroid for rescue, pharmacy visits, ED visits, hospital admission, and the last section about asthma control score. The ACT, a validated tool for assessing control of asthma,[16] was incorporated into the sixth section of the survey.

Participants

All patients with severe asthma receiving biologic therapy under follow-up in the severe asthma clinic ($n = 60$) were invited to participate in this study. After verbal informed consent, patients who agreed to participate were interviewed by experienced clinicians via telephone.

Study outcomes

The subjective impact of the COVID-19 pandemic and lockdown on the control of asthma in this cohort was inferred from participants' reported perception of control of asthma and changes in maintenance medication use. The ACT score was used as an objective assessment of control of asthma. When using the ACT score to evaluate interventions, it has been recommended that a change of 3 points is a minimally important difference (MID, i.e., smallest clinically significant change).[16] The difference in ACT scores was therefore calculated, and the factors associated with changes greater than the MID were assessed.

Patients were also stratified into three groups based on the ACT (uncontrolled [UC] <16, partially controlled [PC] 16–19, and controlled [C] 20–25) as per the Global Initiative for Asthma Guidelines 2019.[17] The objective impact was determined by absolute differences in the ACT scores and changes in number of patients in these strata. To screen for response bias, patients reported time since diagnosis of asthma, duration of biologic therapy, prescription medications, ED visits, and hospital admissions were cross-checked against electronic medical records.

Statistical analysis

Data were entered and analyzed using IBM SPSS Statistics for Windows version 24, IBM Corp. Categorical data are presented as frequencies and percentages, and the marginal homogeneity test or McNemar's Chi-square test was used to compare the marginal proportions' distributions of all categorical data. Numerical data are presented as means ± standard deviation (SD) and compared using Student's *t*-test for paired data. A test with $P < 0.05$ was considered to be statistically significant.

Results

Demographics

Participants' demographic data are shown in Table 1. A total of 56 participants, female 39(69%) ; mean age ± standard deviation 47.4 ± 13.8 years. The majority of participants were Saudi (53, 95%), married (47, 84%), and resident in Riyadh (46, 82%). Most patients had been treated with omalizumab (47, 84%); the rest received mepolizumab (7, 12.5%) and dupilumab (2,

Table 1: Demographic and other clinical characteristics

	n (%)
Age (years)	
22-30	6 (10.7)
31-40	15 (26.8)
41-50	11 (19.6)
51-60	14 (25.0)
61+	10 (17.9)
Gender	
Male	17 (30.4)
Female	39 (69.6)
Highest level of education	
No formal education	9 (17.3)
Elementary	4 (7.7)
Primary	6 (11.5)
High school	11 (21.2)
University	22 (42.3)
Nationality	
Saudi	53 (96.4)
Non-Saudi	2 (3.6)
Employment status	
Employed	21 (41.2)
Unemployed	5 (9.8)
Homemaker	25 (49.0)
Marital status	
Single	5 (9.6)
Married	47 (90.4)
Divorced	1 (1.8)
City of residence	
Riyadh	46 (82.1)
Outside Riyadh	10 (17.9)
Biologics used for severe asthma	
Omalizumab	47 (84)
Mepolizumab	7 (12.6)
Dupilumab	2 (3.6)
Asthma symptoms after curfew and lockdown	
Better	28 (50)
Unchanged	22 (40)
Worse	6 (10)
Duration of asthma since diagnosis (years)	4-30
Duration of biologic therapy (months)	5-120

3.6%). All these patients had been on biologic therapy for >5 months.

Asthma duration, biologic add-on therapy, and use of inhaled bronchodilator and inhaled corticosteroid biological therapy before COVID-19 pandemic

In this cohort, the mean time since diagnosis of asthma was 19.6 years (SD: 11.5 years). The majority of these patients (54, 95%) regularly attended the outpatient clinics for severe asthma under specialist care. Most of the patients agreed that their symptoms of asthma had improved with biologic therapy (45, 80.4%). Their reported use of inhaled bronchodilator and inhaled corticosteroid before the COVID-19 pandemic is detailed in Table 2.

When asked, 28 participants (50%) in this survey reported that their asthma symptoms were better overall during the COVID-19 lockdown period. This statement is supported by the reported reduction in bronchodilator inhaler therapy in 23 (41%) and inhaled steroids in 15 (26.8%) patients

The subjective effects of the COVID-19 pandemic and social distancing on the overall control of participants' asthma are detailed in Table 3.

Asthma control test scores before and after 12 weeks of the COVID-19 lockdown period

As shown in Table 3, participants' mean ACT scores before (17.3 ± SD 4.7) and after 12 weeks of the COVID-19 lockdown (19.7 ± SD 4.5) suggested significant improvement in control of asthma (mean difference: 2.4 ± SD 3.7, $P < 0.001$). Of the 38 (67.9%) participants whose ACT scores increased, 18 (32.1%) achieved the MID (≥ 3 points). Furthermore, 5 of these 38 participants had a remarkable improvement in their ACT scores (≥ 9 points). However, 16 participants' scores (28.6%) did not change, and 2 (3.6%) fell.

Participants' ACT scores stratified into UC, PC, and controlled groups are detailed in Table 4. Importantly, 13 participants improved and joined the controlled group from either the UC (5, 8.9%) or PC (8, 14.3%) group. Three participants (5.4%) improved and joined the PC group from the UC group. However, two participants deteriorated and moved from the controlled group to the PC group. Of these, one, whose ACT score dropped 5 points, had received biologic therapy but, because of side effects (urinary retention and constipation), had stopped other all medications. As a result, she had also needed to visit the ED.

Table 2: Asthma medication use before and after coronavirus disease

Use of bronchodilator and steroid	Before COVID lockdown, n (%)	After COVID lockdown, n (%)	P
Daily use ICS			
Yes	56 (100.0)	55 (98.2)	1
No	0	1 (1.8)	
Frequency of ICS inhaled steroid use			
Twice daily	46 (83.6)	41 (73.2)	0.034
Once daily	6 (10.9)	9 (16.1)	
As needed for symptoms	3 (5.5)	4 (7.1)	
Not using	0	2 (3.6)	
Use bronchodilator?			
Yes	51 (92.7)	47 (92.2)	1
No	4 (7.3)	4 (7.8)	
Delivery of bronchodilator			
Inhaler	41 (78.8)	42 (82.4)	0.67
Nebulizer	4 (7.7)	2 (3.9)	
Both	7 (13.5)	7 (13.7)	
Frequency of inhaled bronchodilator use			
PRN	1 (3.2)	1 (3.2)	0.502
Daily	5 (16.1)	9 (29.0)	
Twice daily	0	2 (6.5)	
Three times or more day	8 (25.8)	2 (6.5)	
Once per month	0 (0.0)	1 (3.2)	
Indication for use of bronchodilator?			
Maintenance therapy for asthma	1 (2.0)	4 (9.3)	0.343
Rescue therapy daily	23 (46.0)	18 (41.9)	
Rescue therapy up to once per week	13 (26.0)	11 (25.6)	
Rescue therapy more than twice per week	13 (26.0)	10 (23.3)	

COVID=Coronavirus disease, ICS=Inhaled corticosteroid, PRN=As needed medication

Table 3: Asthma control before and after lockdown

ACT score strata	Asthma control score based on ACT		P
	Before COVID-19 pandemic, *n* (%)	During lockdown period, *n* (%)	
Uncontrolled ≤15	17 (30.4)	9 (16.1)	0.001
Partially controlled 16-19	16 (28.6)	13 (23.2)	
Controlled ≥20	23 (41.1)	34 (60.7)	

ACT=Asthma control test, COVID-19=Coronavirus disease 2019

Table 4: Asthma control score before and after coronavirus disease

Time point	ACT score, mean±SD	P
Before COVID-19 pandemic	17.3±4.7	<0.001
During COVID-19 lockdown	19.7±4.5	
Difference	2.4±3.7	

ACT=Asthma control test, SD=Standard deviation, COVID-19=Coronavirus disease 2019

The marginal homogeneity test demonstrated a statistically significant difference between the marginal proportions' distributions of these groups ($P = 0.001$) before and after 12 weeks of the lockdown period. Furthermore, the most interesting observation in the study was an increase in the proportion of patients who were controlled before and after 12 weeks of the lockdown (23 [41%] vs. 34 [60.7%]). When all participants whose ACT scores increased were compared with those whose did not, no statistically significant differences in age, gender, employment status, the highest level of education achieved, marital status, difficulty obtaining medications, pharmacy treatment, oral steroid use, ED visits, or failure to receive scheduled biologic therapy were found.

Quality of air and pollution during COVID-19 lockdown period in Riyadh Region, March–June 2020

Riyadh region was lockdown by authorities to contain the spread of COVID-19 virus by imposing strict curfew in March 2020. All traffic and industrial activities were significantly reduced during this lockdown period. The resulting reduction in vehicular and industrial activity led to significant improvement in quality of air and reduced pollution, as shown in Figure 1. Levels of CO, SO_2, and nitrous oxide (NO_2) were all shown to decrease in Riyadh region compared to the months before the lockdown. All these pollutants are directly linked with the traffic and industrial activity in the area. This improvement in quality of air has favorable effects in people with respiratory diseases in general but asthma in particular. Approximately half of the participants (30, 53.6%) believed that the improvement in their asthma was related to reduction in air pollution during the period that social distancing was enforced.

Discussion

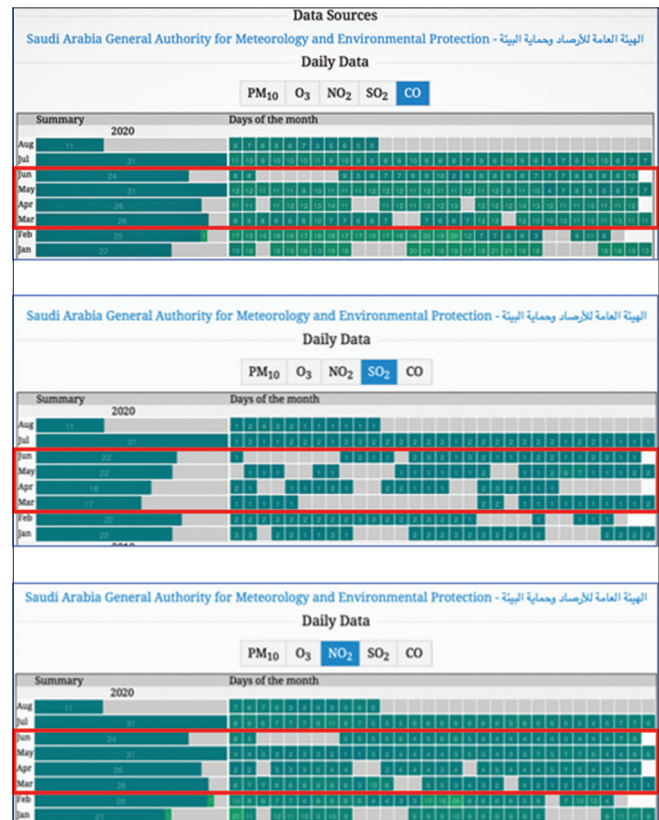The majority of our cohort of patients with severe

Figure 1: Environmental data (carbon monoxide, sulfur dioxide, and NO_2 related to vehicular and industrial activity) for Riyadh region March–June 2020 source: Saudi Arabia General Authority for Meteorology and Environmental Protection

asthma were actively being treated with biologic agents. Half subjectively reported improvement, and a third had a clinically significant improvement in ACT score (≥3points) during the COVID-19 pandemic and enforced social distancing. Furthermore, as defined by their ACT score groups, nearly 25% improved and moved from either the UC or the PC group to the controlled group.

A significant proportion of the reduction in hospitalizations probably reflected improvement in patients' asthma. This improvement occurred as a result of the many psychological, behavioral, environmental, and health-care-related changes that occurred during the 12-week lockdown period. These changes could be considered an "asthma care bundle." This package of interventions resulted in statistically and clinically significant improvement in control of asthma as defined

movement into the controlled ACT score group from another group (i.e., UC or poorly controlled).

The scope of this study cannot exclude other factors that may have been relevant to the improvement of asthma in this cohort. However, environmental control is the most obvious factor that changed over the 12-week period of this study. Atmospheric pollution is a well-recognized precipitant of asthma attacks.[6,14] Reductions in this will probably be relevant.[18] Indeed, the meteorological and environmental report for Riyadh stated that atmospheric pollution fell during the COVID-19 lockdown period due to reduced traffic and industrial activities.[19] While more than 50% of the patients in this study reported an improvement in their asthma symptoms during the lockdown period, more than half attribute this to a reduction in road traffic activities.

March is a spring season in Riyadh and so viral infections and common outdoor allergens such as dust, pollen, and fungal spores are less prevalent in this season. However, reduced exposure to these precipitants as a result of social distancing measures could also be a factor in improvement of symptoms.

The improvement in this cohort could also reflect increased compliance with asthma treatments for fear of getting COVID-19. However, some patients reduced their inhalers while others self-medicated with rescue oral steroids or took over-the-counter medications. The patients in this cohort have significant experience in the self-management of asthma (mean time from diagnosis was over 19 years). Hence, those who self-medicated during the lockdown will probably have used this strategy to avoid hospitalization before the pandemic. Regardless, some of the falls in hospitalizations probably reflected self-management of mild exacerbations of asthma. Other reasons could include reduced exposure to allergens and prevention of transmission of all respiratory viruses during lockdowns.[13]

A single case report describes the course of symptomatic COVID-19 in a 52-year-old man treated with omalizumab for severe allergic asthma.[11] Remarkably, this patient did not develop pneumonia or an exacerbation of asthma. Patients with allergic asthma may have a lower risk of developing severe COVID-19, and omalizumab can enhance immunity against viruses.

Further research to identify the factors which contributed to the reduction in hospitalizations of patients with asthma during the COVID-19 pandemic and social distancing is required.

Strengths and limitations
There is a lack of knowledge about bronchial asthma control during the COVID-19 pandemic. Major strength of this study is the addition of our knowledge about asthma during the current pandemic. Second, it included patients with severe asthma where the effects of environmental changes or social distancing measures may be obvious compared to other less severe asthma. Reported data obtained at interview can be associated with response bias and so its accuracy can be questioned. However, participants' accounts of ED visits, hospital admissions, prescribed medications, and attendance for administration of biologic therapy were consistent with hospital electronic medical records. Studying a clearly defined cohort of patients with severe asthma, attending a specialist clinic, at a single tertiary care center, where biologic agents are regularly prescribed, provided good internal validity. Consequently, external validity and generalizability may be restricted. However, our survey had a high response rate and our institution serves one of the largest caseloads of patients with severe asthma in Saudi Arabia. Our respondents are therefore likely to be representative of patients with severe asthma treated with biologic agents worldwide.

Conclusions
Many of our patients reported improvement in their asthma during the 12-week COVID-19 lockdown period. This subjective improvement is also consistent with objective assessment of control of asthma using the ACT score as well as Emergency Room (ER) visits, hospital admissions, prescription medications, and attendance for their biologic treatment administration. Many of the patients in this survey attribute this improvement to reduction in atmospheric pollution due to reduced road traffic activity during the lockdown period. The data on air pollution in Riyadh during this period would tend to support this.

Ethics approval and consent to participate
This retrospective, observational study was approved by the IRB of the King Abdullah International Medical Research Center, Riyadh, Saudi Arabia.

Availability of data and material
All authors affirm that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned have been explained. The data that support the findings of this study are available from KAMC, Ministry of National Guard – Health Affairs, Riyadh, Saudi Arabia. However, restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of KAMC.

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Conflicts of interest
There are no conflicts of interest.

References

1. Mathew J, Aronow WS, Chandy D. Therapeutic options for severe asthma. Arch Med Sci 2012;8:589-97.
2. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, *et al*. Global asthma prevalence in adults: Findings from the cross-sectional world health survey. BMC Public Health 2012;12:204.
3. Bahadori K, Doyle-Waters MM, Marra C, Lynd L, Alasaly K, Swiston J, *et al*. Economic burden of asthma: A systematic review. BMC Pulm Med 2009;9:24.
4. Barbosa JP, Ferreira-Magalhães M, Sá-Sousa A, Azevedo LF, Fonseca JA. Cost of asthma in Portuguese adults: A population-based, cost-of-illness study. Rev Port Pneumol 2017;23:323-30.
5. Levy ML. The national review of asthma deaths: What did we learn and what needs to change? Breathe (Sheff) 2015;11:14-24.
6. Spann K, Snape N, Baturcam E, Fantino E. The impact of early-life exposure to air-borne environmental insults on the function of the airway epithelium in asthma. Ann Glob Health 2016;82:28-40.
7. Romeo E, de Sario M, Forastiere F, Compagnucci P, Stafoggia M, Bergamaschi A, *et al*. PM 10 exposure and asthma exacerbations in pediatric age: A meta-analysis of panel and time-series studies. Epidemiol Prev 2006;30:245-54.
8. Barone-Adesi F, Dent JE, Dajnak D, Beevers S, Anderson HR, Kelly FJ, *et al*. Long-term exposure to primary traffic pollutants and lung function in children: Cross-sectional study and meta-analysis. PLoS One 2015;10:e0142565.
9. Zheng XY, Ding H, Jiang LN, Chen SW, Zheng JP, Qiu M, *et al*. Association between air pollutants and asthma emergency room visits and hospital admissions in time series studies: A systematic review and meta-analysis. PLoS One 2015;10:e0138146.
10. Novak N, Cabanillas B. Viruses and asthma: The role of common respiratory viruses in asthma and its potential meaning for SARS-CoV-2. Immunology 2020;161:83-93.
11. Lommatzsch M, Stoll P, Virchow JC. COVID-19 in a patient with severe asthma treated with omalizumab. Allergy 2020;75:2705-8.
12. Teach SJ, Gill MA, Togias A, Sorkness CA, Arbes SJ Jr., Calatroni A, *et al*. Preseasonal treatment with either omalizumab or an inhaled corticosteroid boost to prevent fall asthma exacerbations. J Allergy Clin Immunol 2015;136:1476-85.
13. Gupta A, Bush A, Nagakumar P. Asthma in children during the COVID-19 pandemic: Lessons from lockdown and future directions for management. Lancet Respir Med 2020;8:1070-1.
14. Wilder-Smith A, Freedman DO. Isolation, quarantine, social distancing and community containment: Pivotal role for old-style public health measures in the novel coronavirus (2019-nCoV) outbreak. J Travel Med 2020;27:taaa020.
15. Yezli S, Khan A. COVID-19 social distancing in the Kingdom of Saudi Arabia: Bold measures in the face of political, economic, social and religious challenges. Travel Med Infect Dis 2020;37:1-4.
16. Schatz M, Kosinski M, Yarlas AS, Hanlon J, Watson ME, Jhingran P. The minimally important difference of the asthma control test. J Allergy Clin Immunol 2009;124:719-23.e1.
17. Global Initiative for Asthma. Asthma Management and Prevention for Adults and Children Older than 5 Years. Pocket Guide for Health Professionals; 2019. Available from: https://ginasthma.org/wp-content/uploads/2019/04/GINA-2019-main-Pocket-Guide-wms.pdf. [Last accessed on 2020 Jul 28].
18. Künzli N, Kaiser R, Medina S, Studnicka M, Chanel O, Filliger P, *et al*. Public-health impact of outdoor and traffic-related air pollution: A European assessment. Lancet (London, England) 2000;356:795-801.
19. Riyadh's air Pollution Drops Significantly Amid COVID-19 Virus Measures – Saudi Gazette. In: Saudi Gaz; 2020. Available from: https://saudigazette.com.sa/article/593149/SAUDI-ARABIA/Riyadhs-air-pollution-drops-significantly-amid-COVID-19virus-measures. [Last accessed on 2020 Jul 25].