ORIGINAL ARTICLE: ASTHMA

The effect of the COVID-19 lockdown on children with asthma-related symptoms: A tertiary care center experience

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Abstract

Background: Acute asthma exacerbations are a common cause for emergency department (ED) visits and hospitalizations in children. Since the outbreak of coronavirus disease 2019 (COVID-19) and the education system closure/total lockdown in Israel on March 2020, we have noticed a decrease in pediatric ED visits and an increase in hospitalizations of asthma exacerbations.

Objective: to examine the patterns of ED visits for asthma exacerbations during COVID-19 outbreak, in comparison to the previous year.

Methods: A retrospective study comparing asthma related ED visits and hospitalizations among children aged 2–18 years at a tertiary center in southern Israel. Three time periods were selected: 2020 A (prelockdown, 2/1/20 to 3/14/20), 2020 B (lockdown, 3/15/20 to 5/15/20) and 2020 C (postlockdown, 5/16/20 to 6/30/20) and compared to the three parallel time periods in 2019. Data regarding demographics, number of ED visits and clinical severity parameters were collected and analyzed.

Results: Five hundred and twelve children visited the ED for asthma exacerbation: 273 children during 2019 and 239 children during 2020. Lockdown period in 2020 revealed significantly fewer ED visits per day compared to the parallel calendar period in 2019 (1.8 vs. 1.43, p < .001). Significantly higher hospitalization rate (47.1% vs. 33.7%, p = .05) and longer length of stay (3.15 vs. 1.9 days, p = .03) were observed during the lockdown.

Conclusion: Lockdown is associated with fewer ED visits for asthma exacerbation, probably due to; reduced exposure to viral infections and environmental allergens, decreased availability of primary physicians and families’ reluctance to arrive to the ED. ED visits during lockdown were characterized by higher hospitalization rate and longer LOS.

Keywords
asthma, children, COVID-19, emergency department, lockdown

Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; LOS, length of stay; PICU, pediatric intensive care unit.

Inbal Golan-Tripto and Noga Arwas contributed equally to this study.
1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) outbreak has led, since the beginning of 2020, to the implementation of “social distancing” practices including school closures in many countries, to reduce the transmission of the disease. When we analyze the “lockdown approach” during influenza pandemic, a mean reduction of 29.6% in the peak of the epidemic after school closure was reported by a systematic review of 31 studies. Another review presented a substantial reduction of up to 50% in the transmission of disease among children after school closure during influenza outbreak.

To date, children appear to represent a low proportion out of total confirmed COVID-19 cases and are usually asymptomatic or present with mild symptoms.

Asthma is the most common pediatric chronic respiratory disease. Acute exacerbations continue to be a major health concern among children worldwide and a common reason for emergency department (ED) visits and hospitalizations in the pediatric age. In a study examining asthma-related ED visits and hospital admissions in the United State between 2010 and 2015, acute asthma exacerbations accounted for 3% of ED visits and 6% of hospital admissions among children aged 5–17 years. Respiratory tract infections and allergens exposure have been recognized as the most common triggers for asthma exacerbations in children, with suggested synergistic interactions between these factors. The seasonal pattern of asthma exacerbations is well established. A typical peak is in September, when children return to school after the summer break. In school-aged children, another peak has been viewed during the spring months, that can be attributed to the spread of pollen allergens, also known as a trigger for asthma exacerbation in this age group. There is scarcely any data on whether childhood asthma constitutes a risk factor for COVID-19 severity.

Recent data suggests blood eosinophil counts may have a prognostic value in COVID-19, with eosinopenia indicating a severe disease.

Since the introduction of the COVID-19 outbreak and education system closure in Israel on March 15, 2020, we have noticed a decrease in pediatric ED visits, specifically for asthma related visits, comparing to previous years. Similar observations were recently reported with a decline of 76% in the asthma related ED visits, and a lower hospitalization rate, during COVID-19 lockdown.

Therefore, we aim to examine the patterns of pediatric ED visits for asthma exacerbations during the COVID-19 outbreak, pre-lockdown, during lockdown and post lockdown, in comparison to the previous year.

2 | METHODS

This is a descriptive, cross-sectional study, comparing the asthma related ED visits and hospital admissions in Soroka University Medical Center, a single tertiary center in southern Israel, among children aged 2-18 years. Three time periods were selected: 2020 A (pre-lockdown, 2/1/20 to 3/14/20), 2020 B (lockdown, 3/15/20 to 5/15/20) and 2020 C (post-lockdown, 5/16/20 to 6/30/20) and were compared to three parallel time periods in 2019.

2.1 | Patients

Pediatric patients aged 2–18 years that presented to the ED during one of the selected time periods for asthma related symptoms (e.g., shortness of breath, wheezing, tachypnea), and were treated during the visit with anti-asthmatic medications, were included in the study. Using electronic health record data, we collected the parameters for each patient, including relevant medical history and medications. Data collected included: demographic data, chronic diagnoses, medications prescribed, vital signs on admission, radiological findings, treatment at the ED, triage acuity during presentation according to Canadian Triage assessment score, pediatric ward or pediatric intensive care unit (PICU) admissions and length of hospitalization stay (LOS). The study received the approval of the institutional ethics committee (No. 184-20).

Our primary outcome was number of visits to the ED for asthma related symptoms during 2020 A, 2020 B and 2020 C, in comparison to 2019 A, 2019 B and 2019 C. Our secondary outcomes were clinical severity parameters during the visits, indicated by vital signs, radiology findings, rate of hospitalizations, rate of hospitalizations in PICU, LOS and LOS in the PICU. We hypothesized significantly fewer visits during lockdown, with higher severity parameters. We expected increase in ED visits after the lockdown, similar to the “September pandemic,” after summer vacation.

2.2 | Statistical analysis

Comparisons of demographic, clinical and chest X-ray imaging as well as outcomes of admissions were performed with appropriate univariate analyses. Specifically, nominal variables were compared using Pearson’s χ² test, continuous variables that matched parametric criteria were compared by using Student’s t test or one-way analysis of variance, and ordinal variables and continuous variables that did not match parametric criteria were compared by using Wilcoxon or Mann–Whitney U tests. Continuous variables are presented as mean ± SD. Categorical data are expressed as percentages. Statistical significance was defined as p ≤ .05. Analyses were performed via IBM SPSS software version 22.

3 | RESULTS

A total of 512 children presented to the ED for asthma related symptoms during the study periods: 273 children during 2019 (124 in 2019 A, 89 in 2019 B and 60 in 2019 C) and 239 children during 2020 (125 in 2020 A, 51 in 2020 B and 63 in 2020 C). Demographic data were similar except for their age, which was younger during
| TABLE 1  | Demographic, chronic diagnoses, and chronic medications |
|-----------------|----------------------------------------------------------|
|                | 2019 A | 2019 B | 2019 C | 2020 A | 2020 B | 2020 C Post lockdown | p value for 6 periods | p value for comparison of 2019 versus 2020 |
| Age, years Mean ± SD | 6.75 ± 4.38 | 6.71 ± 4.47 | 6.08 ± 4.14 | 7.38 ± 4.15 | 7.96 ± 4.75 | 8.22 ± 5.23 | .060 | .002 |
| Male, n (%) | 71 (58.2%) | 56 (63.6%) | 39 (66.1%) | 65 (52.8%) | 27 (54.0%) | 40 (64.5%) | .384 | .207 |
| Ethnicity, n (%) | | | | | | | | |
| Bedouins | 99 (79.8%) | 54 (60.7%) | 37 (61.7%) | 79 (63.2%) | 40 (78.4%) | 41 (65.1%) | .002 | .032 |
| Non-Bedouins | 25 (20.2%) | 35 (39.3%) | 23 (38.3%) | 46 (36.8%) | 11 (21.6%) | 22 (34.9%) | | |
| Chronic diagnoses, n (%) | | | | | | | | |
| Atopy | 2 (1.6%) | 1 (1.1%) | 1 (1.7%) | 0 (0.0%) | 1 (2.0%) | 1 (1.6%) | .690 | .614 |
| Premature birth | 1 (0.8%) | 1 (1.1%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | .501 | .612 |
| Pulmonary HTN. | 3 (2.4%) | 0 (0.0%) | 1 (1.7%) | 1 (0.8%) | 0 (0.0%) | 0 (0.0%) | .378 | .291 |
| OSA, Upper airway obstruction | 1 (0.8%) | 2 (2.2%) | 2 (3.3%) | 3 (2.4%) | 0 (0.0%) | 0 (0.0%) | .729 | .326 |
| BPD | 2 (1.6%) | 0 (0.0%) | 0 (0.0%) | 1 (0.8%) | 0 (0.0%) | 0 (0.0%) | 1.000 | .454 |
| Chronic respiratory diagnosis | 6 (4.8%) | 289 (22.2%) | 2 (3.3%) | 5 (4.0%) | 0 (0.0%) | 0 (0.0%) | .293 | .119 |
| Chronic non-respiratory diagnosis | 15 (12.1%) | 10 (11.2%) | 9 (15.0%) | 13 (10.4%) | 5 (9.8%) | 6 (9.5%) | .390 | .934 |
| Chronic treatment, n (%) | | | | | | | | |
| ICS | 14 (11.3%) | 8 (9.0%) | 10 (16.7%) | 10 (8.0%) | 5 (9.8%) | 5 (7.9%) | .210 | .538 |
| LABA | 1 (0.8%) | 1 (1.1%) | 2 (3.3%) | 3 (2.4%) | 3 (5.9%) | 3 (4.8%) | .099 | .327 |
| SABA | 2 (1.6%) | 0 (0.0%) | 3 (5.0%) | 3 (2.4%) | 4 (7.8%) | 1 (1.6%) | .277 | .068 |
| LTRA | 4 (3.2%) | 4 (4.5%) | 2 (3.3%) | 3 (2.4%) | 2 (3.9%) | 1 (1.6%) | .455 | .921 |
| Chronic respiratory treatment | 16 (12.9%) | 11 (124%) | 11 (18.3%) | 11 (8.8%) | 7 (3.7%) | 6 (9.5%) | .180 | .539 |
| Chronic non-respiratory treatment | 22 (17.7%) | 10 (11.2%) | 12 (20.0%) | 14 (11.2%) | 3 (5.9%) | 4 (6.3%) | .013 | .060 |

Abbreviations: BPD, bronchopulmonary dysplasia; HTN, hypertension; ICS, inhaled corticosteroids; LABA, long acting beta agonist; LTRA, leukotriene receptor antagonist; OSA, obstructive sleep apnea; SABA, short acting beta agonist.
The number of visits per day increased significantly in the era after lockdown when comparing 2020 C to 2020 B (2 vs. 1.43 visits per day, \( p < .001 \)) as well as when compared to the same time period in 2019 (2 vs. 1.76 visits per day \( p < .001 \)) (Table 3).

During lockdown, hospitalization rate was higher (47.1% vs. 33.7%, \( p = .05 \)) as was length of stay (3.15 vs. 1.9 days, \( p = .03 \)), possibly indicating higher severity (Figure 1B). Only six patients were admitted or transferred to the PICU during six time periods, four of them necessitated high flow nasal cannula ventilation. There was no difference in PICU admissions rate or LOS in PICU, between time periods.

### 4 | DISCUSSION

In this descriptive cross-sectional study, including 512 children who presented to the ED for asthma related symptoms during three time periods in two consecutive years, we demonstrated different patterns in ED visits and in hospitalizations during pre-lockdown, lockdown and post lockdown periods, compared with 2019.

There was no difference in the demographic data between the groups except for trend towards older age during 2020 compared with 2019. Male predominance, as can be expected among this pre-pubertal age group, was observed. The majority of our patients during all time periods were of Bedouin Arab descent, with a significant increase in their visits during lockdown. This could be explained by the low socioeconomic status of the Bedouin population in southern Israel, some which are living in large families with overcrowding, poor accommodations/housing conditions, and limited access to health care in some of the settlements.

In those areas, social distancing is more difficult to achieve and the exposure to outdoor allergens was probably not significantly reduced, even during the lockdown. The mildly lower heart rate and respiratory rate noticed in 2020 is clinically insignificant and could stem from the difference in patients age between 2019 and 2020, with an average of 1.5 years older in 2020. Since asthma severity parameters (hospitalization rate and LOS) were higher during 2020 B, we can assume that this change in vital signs did not reflect milder cases, but probably proportionate to an older age. Treatment in the ED was similar between all time periods except for a significant drop in the use of NACL 0.9% inhalations during 2020 B and 2020 C. Since the viral infection transmission by reducing the spread of aerosol mass by small-volume nebulizers.

The accumulating evidence on the impact of COVID-19 pandemic on ED visits patterns, show a substantial decrease in the volume of patients presenting to the ED during the pandemic, throughout various disciplines and countries. Furthermore, there are increasing reports on higher hospital admission rates, indicating higher acuity patients, with increased morbidity and mortality due to delayed medical care in non-COVID-19 emergency conditions.
In this descriptive cross-sectional study, we compare three parallel time periods during two consecutive years, and show a significant decrease in pediatric asthma related ED visits during COVID-19 lockdown. Similar trends in asthma related ED visits were observed in different countries, and possible explanations were suggested by the different authors.13,23–26 Since the major triggers for asthma exacerbation in the pediatric population are viral infections, it was expected that social distancing measures during lockdown will decrease viral infections transmission, including Influenza virus, Rhinovirus and Respiratory syncytial virus.27,28 Another important trigger is outdoor exposure to pollen allergens and air pollution,29 again substantially reduced due to minimal exposure during lockdown and the reduction of industrial work.30 Reduced physical activity during lockdown was described in large

### TABLE 2  Vital signs, and radiological findings at the ED

| ED measurements | 2019 A | 2019 B | 2019 C | 2020 A Pre-lockdown | 2020 B Lockdown | 2020 C Post-lockdown | p value for 6 periods | p value for comparison of 2019 versus 2020 |
|-----------------|--------|--------|--------|---------------------|----------------|---------------------|----------------------|----------------------------------------|
| ED Urgency      | 3      | 3.5    | 3      | 3                   | 4              | 3                   | .231                 | .072                                   |
| Min, max        |        |        |        |                     |                |                     |                      |                                        |
| BP systolic     | 110.31 ± 12.44 | 110.93 ± 10.72 | 106.77 ± 12.71 | 110.76 ± 12.31 | 108.47 ± 14.34 | 112.18 ± 13.87 | .298                 | .518                                   |
| Mean ± SD       | 110.43 | 109.0  | 108.0  | 110.0               | 108.0          | 112.0               |                      |                                        |
| Median          |        |        |        |                     |                |                     |                      |                                        |
| BP diastolic    | 67.35 ± 11.75 | 66.69 ± 10.32 | 65.85 ± 10.11 | 68.04 ± 11.82 | 65.95 ± 9.87 | 68.98 ± 11.14 | .663                 | .363                                   |
| Mean ± SD       | 67.0   | 66.0   | 64.0   | 69.5                | 67.0           | 70.0                |                      |                                        |
| Median          |        |        |        |                     |                |                     |                      |                                        |
| HR              | 128.74 ± 25.01 | 124.38 ± 22.33 | 124.76 ± 20.77 | 128.49 ± 23.51 | 118.84 ± 23.71 | 118.42 ± 26.58 | .039                 | .231                                   |
| Mean ± SD       | 129.0  | 129.0  | 126.0  | 128.0               | 118.5          | 115.0               |                      |                                        |
| Median          |        |        |        |                     |                |                     |                      |                                        |
| RR              | 34.18 ± 12.05 | 33.13 ± 12.59 | 35.69 ± 12.58 | 32.10 ± 15.03 | 29.00 ± 11.13 | 31.19 ± 13.26 | .005                 | <.001                                  |
| Mean ± SD       | 32.04  | 32.0   | 30.0   | 28.0                | 26.0           | 26.0                |                      |                                        |
| Median          |        |        |        |                     |                |                     |                      |                                        |
| SAT             | 95.98 ± 4.86 | 96.73 ± 3.33 | 95.22 ± 5.68 | 96.07 ± 3.85 | 96.86 ± 3.98 | 97.27 ± 3.49 | .077                 | .201                                   |
| Mean ± SD       | 97.00  | 98.00  | 97.00  | 97.00               | 98.00          | 99.00               |                      |                                        |
| Median          |        |        |        |                     |                |                     |                      |                                        |
| SAT (in hospitalized patients) | 92.28 ± 6.17 | 94.10 ± 4.20 | 91.50 ± 6.55 | 93.60 ± 4.15 | 94.92 ± 4.97 | 95.39 ± 4.10 | .117                 | .066                                   |
| Mean ± SD       | 94.00  | 95.00  | 93.00  | 94.00               | 96.50          | 95.50               |                      |                                        |
| Median          |        |        |        |                     |                |                     |                      |                                        |
| Temperature     | 37.71 ± 1.11 | 37.54 ± 0.92 | 37.28 ± 0.75 | 37.59 ± 0.90 | 36.64 ± 1.08 | 37.32 ± 0.77 | .100                 | .959                                   |
| Mean ± SD       | 37.00  | 37.00  | 37.00  | 37.00               | 37.00          | 37.00               |                      |                                        |
| Median          |        |        |        |                     |                |                     |                      |                                        |
| Hyperinflation chest X-ray, n (%) | 26 (21.0%) | 14 (15.7%) | 14 (23.3%) | 23 (18.4%) | 7 (13.7%) | 12 (19.0%) | .523                 | .758                                   |
| Atelectasis/ filtration, n (%) | 11 (8.9%) | 12 (13.5%) | 10 (16.7%) | 12 (9.6%) | 6 (11.8%) | 3 (4.8%) | .255                 | .306                                   |

Abbreviations: BP, blood pressure; ED, emergency department; HR, heart rate; RR, respiratory rate; SAT, oxygen saturation.
questionnaires studies, along with an increase in children's psychological and behavioral symptoms and elevated screen-time. Socioaffective complications and insufficient physical activity were underscored as two of the main concerns, particularly among socioeconomic deprived children. As a result, a reduction in physical activity reduces the number of asthma exacerbations related to exercise induced bronchospasm and exercise induced asthma. The fewer ED visits during lockdown can also result from better asthma control while the parents are at home, providing better adherence to anti asthmatic controllers therapy. Although, this issue is most probably of limited effect, since most of the parents that participated in a telephone visit during lockdown, stated they stopped the preventive therapy as their child was feeling well. Another issue that should be discussed is the avoidance of approaching for medical care when it’s not necessary.

| ED treatments | 2019 A | 2019 B | 2019 C | 2020 A Pre-lockdown | 2020 B Lockdown | 2020 C Post-lockdown | p value for 6 periods | p value for comparison of 2019 versus 2020 |
|---------------|--------|--------|--------|---------------------|-----------------|---------------------|---------------------|----------------------------------------|
| Oxygen, n (%) | 31 (25.0%) | 13 (14.6%) | 11 (18.3%) | 36 (28.8%) | 11 (21.6%) | 16 (25.4%) | .096 | .207 |
| SABA, n (%)   | 52 (41.9%) | 42 (47.2%) | 34 (56.7%) | 63 (50.4%) | 15 (29.4%) | 27 (42.9%) | .503 | .063 |
| Antihistamines, n (%) | 0 (0.0%) | 1 (1.1%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1.000 | .622 |
| Anti-cholinergic inhalations*, n (%) | 40 (32.3%) | 34 (38.2%) | 30 (50.0%) | 42 (33.6%) | 11 (21.6%) | 24 (38.1%) | .165 | .050 |
| ICs, n (%)    | 2 (1.6%) | 3 (3.4%) | 2 (3.3%) | 2 (1.6%) | 0 (0.0%) | 1 (1.6%) | .350 | .625 |
| Steroids PO, n (%) | 36 (29.0%) | 25 (28.1%) | 21 (35.0%) | 33 (26.4%) | 10 (19.6%) | 18 (28.6%) | .256 | .617 |
| Steroids IV, n (%) | 3 (2.4%) | 3 (3.4%) | 4 (6.7%) | 8 (6.4%) | 2 (3.9%) | 5 (7.9%) | .171 | .496 |
| Antibiotics*, n (%) | 7 (5.6%) | 11 (12.4%) | 3 (5.0%) | 8 (6.4%) | 5 (9.8%) | 0 (0.0%) | .307 | .018 |
| Sodium chloride inhalation*, n (%) | 60 (48.4%) | 43 (48.3%) | 35 (58.3%) | 65 (52.0%) | 10 (19.6%) | 14 (22.2%) | .002 | <.001 |

**Clinical severity outcomes**

| ED visits, n (%) | 124 | 89 | 60 | 125 | 51 | 63 |
|------------------|-----|----|----|-----|----|----|
| ED visits per day* | 3.32 | 1.80 | 1.76 | 3.07 | 1.43 | 2.00 |
| Mean ± SD        | ±1.93a | ±0.93b | ±0.78c | ±1.71a,d,e | ±0.65b,d,f | ±1.15c,e,f |
| Patient hospitalized, n (%) | 43 (34.7%) | 30 (33.7%) | 24 (40.0%) | 53 (42.4%) | 24 (47.1%) | 28 (55.6%) | .44 | .05 |
| LOS, days*       | 2.28 ± 1.68 | 1.97 ± 1.98 | 3.45 ± 4.15 | 2.07 ± 2.951 | 3.15 ± 3.23d | 1.30 ± 0.81e | .03 | .12 |
| Mean ± SD        | 1.02 | 1.02 | 1.02 | 1.02 | 1.02 | 1.02 |
| Hospitalized in PICU, n (%) | 1 (0.8%) | 2 (2.2%) | 1 (1.7%) | 1 (0.8%) | 0 (0.0%) | 1 (1.6%) | .79 | .69 |
| LOS in PICU, days | 12.79 | 4.57 | 1.33 | 21.08 | 0 | 1.04 |
| Mean ± SD        | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 |

*Represent parameters with p < .05. Bold p values also represent p < .05.

Abbreviations: ED, emergency department; ICs, inhaled corticosteroids; LOS, length of stay; NS, not significant; PICU, pediatric intensive care unit; PO, per os; SABA, short acting beta agonist.

aComparison between 2019 A and 2020 A periods, p value NS.
bComparison between 2019 B and 2020 B periods, p value NS.
cComparison between 2019 C and 2020 C periods, p value NS.
dComparison between 2020 A and 2020 B periods, p < .001.
eComparison between 2020 A and 2020 C periods, p < .01.
fComparison between 2020 B and 2020 C periods, p value NS. Patients hospitalization.
gComparison between 2019 A and 2020 A periods, p value NS.
hComparison between 2019 B and 2020 B, p value NS.
iComparison between 2019 C and 2020 C periods, p value NS. Length of stay.
During lockdown, due to concerns of parents from increased exposure and the risk of COVID-19 transmission.

After lockdown, we demonstrated significant rise in number of ED visits, even in comparison to same time period during the previous year. In Israel, children younger than 12 years of age returned back to school after lockdown, while adolescences (aged 12–18 years) attended home school program. When we looked at the subgroup of children aged 12–18 years, the visit’s numbers were similar between different study periods. That fact actually correlates with our hypothesis that everyday exposure to classmates is one of the major triggers for asthma exacerbation, and because this age group was in home schooling program during 2020 C, it was not affected by lockdown opening. We speculate that post lockdown rise represents the return to routine activity with everyday exposure to classmates, outdoor pollen exposure, rise in air pollution and physical activity, especially in the younger sub-group, aged 2–12 years. This may resemble “September pandemic,” when children returning to school after summer vacations with significant rise in asthma exacerbations.8

Alongside with a significant reduction in ED visits for asthma exacerbations during lockdown, higher hospitalization rates and longer LOS were observed, that may indicate more severe exacerbations predominate this period. This observation could be attributed to delay in presentation both due to reduced availability of community health care services and the concern of lack of proper follow-up in the community.

Our study has a few limitations. This is a single tertiary center experience, and therefore can be influenced, as mentioned, by the unique demographics in the region. Another limitation is the retrospective nature of our study, with all data drawn from electronic files. We did not capture data regarding viral PCR in nasal swabs, which could emphasize the role of viral infections as a trigger for exacerbation during different study periods. Some of the data that was documented in a hard copy, in extremely acute patients treated in the resuscitation room, may be missing in the electronic files (e.g., intravenous Magnesium Sulfate).

In conclusion, we report a new pattern of ED visits and hospital stay of children with asthma related symptoms, associated with the COVID-19 pandemic, that perhaps is not only confined to asthma. Pediatricians should be aware to this phenomenon at the community and hospital levels.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS
Inbal Golan-Tripto completed conceptualization (lead); investigation (lead); methodology (lead); project administration (lead); writing original draft (lead); writing review and editing (lead). Noga* Arwas completed conceptualization (equal); investigation (equal); writing original draft (equal); writing review and editing (lead). Michal Maimon and Micha Aviram completed methodology (equal); supervision (equal); writing review and editing (equal). Romi Bari completed data curation (lead); formal analysis (lead); methodology (equal); writing review and editing (equal). Dvir Gatt completed investigation (equal); methodology (equal); writing review and editing (equal).

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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