Original Article

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Air pollution, including PM_{10}, as a potential risk factor for the development of appendicitis in Korea: a case-crossover study

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Objectives: Interest in the association between particulate air pollution and appendicitis risk has been increasing in recent years, and previous studies have suggested a link between particulate matter ≤ 10 μm in diameter (PM_{10}) and appendicitis. However, robust evidence is currently lacking. This study explored the association between short-term PM_{10} exposure and appendicitis using data from Ewha Womans University Mokdong Hospital, Seoul, Korea, between January 1, 2001 and December 31, 2018.

Methods: We employed a time-stratified case-crossover design using data from 6,526 appendicitis patients taken from the hospital's electronic medical records system. We analyzed the data using a conditional logistic regression model adjusted for daily mean temperature and relative humidity. The effect size of PM_{10} was estimated in terms of each 10 $\mu m/m^3$ increase in PM_{10} concentration. Sex, season, and age group were analyzed as subgroups.

Results: Appendicitis patients had been exposed to higher levels of PM_{10} concentrations 3 days (OR 1.045, 95% CI : 1.007–1.084) and 7 days (OR, 1.053; 95% CI, 1.005–1.103) before hospital admission. The case-crossover analysis stratified by sex, age, and season showed that the male sex, being aged under 10, and the cold season were associated with a significantly stronger association between appendicitis and PM_{10} concentrations.

Conclusion: Our study found that PM_{10} concentrations were associated with appendicitis in boys aged under 10. The cold season was also a risk factor. Further research with a larger sample size and with other pollutants is required to clarify the association between PM_{10} and appendicitis.

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Air pollution; Appendicitis; Cross-over studies; Particulate matter; Republic of Korea

Introduction

Background

Globally, acute appendicitis affects 1.17 individuals per 1,000 population annually, with a lifetime risk of 8.6% for men and 6.7% for women [1]. In Korea, the incidence rate is 2.27 per 1,000 population [2]. Although numerous studies have explored the pathogenetic roles of various infectious agents in appendicitis, including viral, bacterial, fungal, and parasitic organisms, there is still no consensus on specific causes [3]. A recent study examining the pathological evidence of appendicitis suggests that pressure in the appendix lumen increases due to the proliferation of intestinal bacteria following lumen obstruction and the accumulation of secreted mucus, leading to pain around the navel [4]. However, this does not account for the initial surge in intestinal bacteria that triggers acute appendicitis. It is believed that this increase may be due to immunological changes or environmental factors, rather than the onset of any specific disease state. The incidence of appendicitis in Western countries rose from the 19th to the early 20th century and then declined after the mid to late 20th century [5]. To explain these historical fluctuations, particulate matter ≤10 μm in diameter (PM_{10}) has been hypothesized as a potential risk factor associated with an increased incidence of appendicitis. Previous studies have also investigated the link between air pollution and appendicitis [6,7].

PM_{10} is defined as fine dust composed of particles ≤10 μm in diameter and is one of the most well-known air pollutants, along with fine particulate matter ($PM_{2.5}$), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3), and carbon monoxide (CO). Since the Korean peninsula is exposed to relatively high levels of PM_{10} due to geopolitical reasons, the health effects of PM_{10} on the population have become particularly apparent in recent years [8]. Previous studies have shown that short-term exposure to pollutants can trigger inflammatory processes, potentially contributing to the development of appendicitis [9].

Objectives

We aimed to clarify the association between PM_{10} exposure and the risk of appendicitis to provide better evidence for developing PM_{10} regulation policies and to alleviate the disease burden caused by appendicitis.

Methods

Ethics statement

This study was reviewed and approved by the Ewha Womans University Mokdong Hospital Institutional Review Board (IRB File No: SEUMC 2020-08-026). The requirement for informed consent was waived.

Study design

We conducted a time-stratified case-crossover study design by linking the PM_{10} level during the case event (the date of hospitalization) to each appendicitis case. The study was described according to the STROBE statement, available at https://www.strobe-statement.org/.

Setting

The electronic medical records of all patients diagnosed with acute appendicitis and hospitalized at Ewha Womans University Mokdong Hospital over an 18-year period were collected. Additionally, national Korean air pollution data for the same period were gathered.

To derive time-stratified matched control events (when no admission occurred), we selected control period dates using the same year, month, and day of the week as the appendicitis hospitalization date, but from different weeks. These lags in exposure were referred to as same-day exposure and exposure lagged by "n days" before the event. The control events were matched with case events on the same day of the week to avoid time trend bias associated with specific weekdays.

Since this study employed a case-crossover analysis, intra-individual comparisons were conducted without accounting for the confounding effects of other risk factors, such as a patient's lifestyle [10]. Instead, we focused on weather variables as potential confounding factors, including daily mean temperature and relative humidity.

Participants

We collected data from 9,886 patients treated for appendicitis at Ewha Womans University Mokdong Hospital, a tertiary medical center in the western part of Seoul, Korea, from January 1, 2001, to December 31, 2018. The information gathered included registration number, gender, age, number of hospitalization days, admission and discharge dates, and residential address. Appendicitis is classified under the International Classification of Disease (ICD) ninth revision (ICD-9) codes 540.9, 540.0, 540.1, or 10th revision (ICD-10) codes K35.0, K35.1, K35.9, along with the in-hospital surgery code 470.

Exclusion criteria

Patients were excluded if they had two or more duplicate records of surgical treatments or if their only surgical records were from the first visit (n=1,107). Additionally, patients were excluded if they had missing data on sex, age, hospitalization date, and/or address (n=1,100). Finally, those missing data on the case period, specifically the date of hospitalization due to appendicitis, were also excluded (n=1,153). This resulted in a total of 6,526 patients being included in the final analysis (Fig. 1).

Variables (study outcomes)

The primary outcome was the PM_{10} exposure level at the time of appendicitis diagnosis.

Data sources and measurement

AirKorea (national air pollution surveillance network) database

Korea's metropolitan area spans 11,861 km^2 and includes Seoul, Incheon, and Gyeonggi-do Provinces. In 2018, 133 monitoring stations were established throughout this region. These stations are part of a national air pollution surveillance network known as "AirKorea," which oversees 240 measurement branches nationwide (https://www.airkorea.or.kr/). The AirKorea database records hourly mean concentrations of air pollutants from continuous monitoring stations, and calculates daily mean and maximum values. PM_{10} measurements were conducted using the beta-ray absorption method, as detailed in previous studies [11]. We linked the exposure data from these monitoring stations to the nearest administrative area corresponding to each patient's residential location. For the two-pollutant model, data were also collected on four additional air pollutants: SO_2, NO_2, CO, and O_3. To assess the effect size and perform sensitivity analysis, we gathered $PM_{2.5}$ measurement data from 2015 to 2018.

Meteorological data from the Korea Meteorological Administration

Meteorological data, including the daily mean values of PM_{10}, temperature, and humidity, were obtained from the Korea Meteorological Administration (http://www.kma.go.kr).

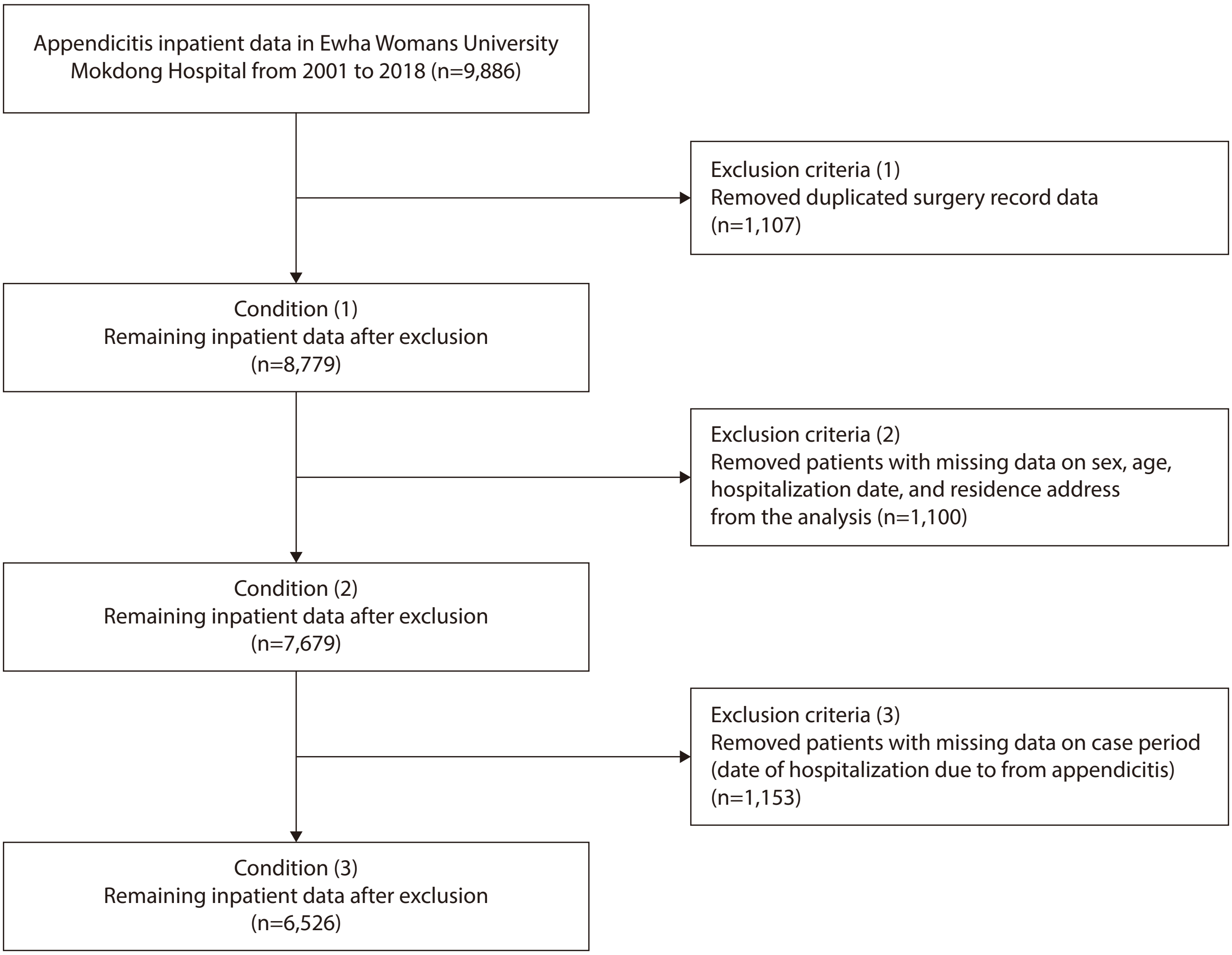

Fig. 1. Identification of appendicitis cases at Ewha Womans University Mokdong Hospital during 2001–2018.

Bias

There was no selection bias reportable in this study.

Study size

Sample size estimation was not performed because this study included all target patients who met the exclusion criteria.

Statistical methods

We analyzed the association between PM_{10} exposure and acute appendicitis using conditional logistic regression (CLR), which is an expanded logistic regression method that accounts for several control periods. This model is particularly effective for case-crossover studies as it accommodates the matched case and control periods within each subject. The CLR model is beneficial in this context because it extends the logistic regression framework to accommodate matched case-control data. This allows for the estimation of exposure-outcome associations while considering the matching structure of the data. Specifically, the CLR model calculates the OR for the occurrence of an event following exposure, taking into account the individual matching factors [10]. For each case of appendicitis, we matched the day of the appendicitis event with four control periods at weekly intervals, ranging from one to four weeks prior to the event. We then calculated ORs with 95% CIs to assess the relationship between an increase in the interquartile range of PM_{10} levels and the incidence of appendicitis.

We analyzed both the single lag effects (from lag 0 to lag 14) and the moving-average effects (from lag 0–1 to lag 0–14). Subgroup analyses were conducted based on sex (boys/girls), season (warm season: April–September; cold season: October–December), and age groups (under 10, 10–19, 20–29, 30–39, 40–49, 50–59, and 60 years or older). The seasonal categorization reflects the climatic patterns typical of Korea. The selection of specific lag periods was informed by the biological likelihood that the inflammatory response to air pollution exposure could manifest within a few days.

We calculated Spearman's correlation between air pollutants before conducting the two-pollutants model. Pairs of exposure variables that demonstrated a high correlation coefficient (greater than 0.7) were excluded from this analysis. In the two-pollutant model, PM_{10} was set as the main exposure while other air pollutants (SO_2, NO_2, CO, and O_3) were adjusted respectively.

When considering the delay between the actual case date and the date of hospitalization, we calculated the PM_{10} concentrations on the hospital admission day and for 7 and 14 days before admission to evaluate the cumulative effect over several days. The ORs for temperature and humidity were also adjusted and we included the daily average humidity and temperature as confounding variables. The lag effect of exposure considered the moving-average effect. The main results were for those on the The main results were for those on the same-day, 3 day, 7 day, and 14 day moving averages. All the data preprocessing and statistical analysis were performed using R statistical software (Ver. 4.0.0, R Development Core Team, Vienna, Austria) and SAS 9.4 (SAS Institute, Cary, NC, USA), and the α level for statistical significance was 0.05.

Results

Participants' demographic and clinical characteristics

A total of 6,526 appendicitis patients were included in the analysis after excluding those with insufficient essential information, such as duplicated, missing, or unmatched data (Fig. 1). The majority of the study participants resided in Seoul, with the administrative areas detailed in Supplement 1. Overall, 51.09% of the study subjects were male (Table 1); however, gender did not significantly influence the risk of appendicitis (P=0.7141). Analysis of age groups revealed that individuals aged 10–19 years (20.85%) were most susceptible to appendicitis, while those aged 60 years and older (8.99%) were least susceptible. Nonetheless, no significant association was found between age and the risk of appendicitis. The number of appendicitis patients hospitalized during the cold season (52.94%) was higher compared to those admitted in the warm season (47.06%). However, no significant association was observed between the season and the risk of appendicitis (P=0.7408).

Levels of environmental exposure in the case and control periods

Table 2 presents the summary statistics for the exposure data collected during the 2001–2018 study period. We assessed the level of environmental exposure in the case and control groups using the t-test and observed no significant difference in PM_{10} levels between the case and control periods. Supplement 2 contains the summary statistics for daily air pollutant exposure levels measured throughout the study period.

Table 1. Descriptive statistics of the epidemiological characteristics of appendicitis patients (n=6,526) at Ewha Womans University Mokdong Hospital during the study period (2001–2018)

Patients' characteristics	Number of patients (%)	OR (95% CI)	P-value
Sex			
Female	3,192 (48.91)	Ref.	0.7141
Male	3,334 (51.09)	1.011 (0.954–1.072)	
Age, yr			
Age (mean±SD)	31.93±19.08		
<10	704 (11.22)	0.972 (0.853–1.106)	0.6649
10–19	1,308 (20.85)	0.992 (0.884–1.113)	0.8866
20–29	1,066 (17.00)	0.981 (0.870–1.105)	0.7473
30–39	1,189 (18.96)	1.004 (0.893–1.129)	0.9507
40–49	851 (13.57)	0.999 (0.881–1.132)	0.9828
50–60	590 (9.41)	0.999 (0.872–1.145)	0.9932
≥60	564 (8.99)	Ref.	
Season			
Warm season	3,071 (47.06)	Ref.	0.7408
Cold season	3,455 (52.94)	1.010 (0.953–1.071)	

Table 2. Summary statistics for daily exposure variables during the study period (2001–2018)

Exposure variables	Case periods (n=6,526)		Control periods (n=14,539)		Mean difference	95% CI	P-value
	Mean	SD	Mean	SD			
PM$_{10}$ (μg/m^3)	53.31	30.68	52.70	29.43	−0.61	(−1.48, 0.26)	0.19
Mean temperature (°C)	13.41	13.16	13.49	13.32	0.08	(−0.23, 0.38)	0.63
Mean humidity (%)	61.41	15.00	61.48	14.97	0.07	(−0.37, 0.51)	0.75

PM$_{10}$, particulate matter ≤10 μm in diameter.

Case-crossover analysis: association between PM$_{10}$ exposure and the risk of appendicitis

Table 3 summarizes the results of the case-crossover analysis examining the association between PM$_{10}$ exposure and the risk of appendicitis. The analysis found an association between the risk of appendicitis and the average PM$_{10}$ concentrations 3 days (OR, 1.045; 95% CI, 1.007–1.084) and 7 days (OR, 1.053; 95% CI, 1.005–1.103) prior to hospital admission. However, no association was observed with PM$_{10}$ concentrations on the day of admission or 14 days before admission.

Sex differences: In male patients, the risk of appendicitis was significantly associated with the mean PM$_{10}$ concentrations 3 days (OR, 1.076; 95% CI, 1.023–1.132) and 7 days (OR, 1.103; 95% CI, 1.035–1.176) prior to admission. However, no significant association was observed in female patients at any lag time.

Age differences: Only patients under the age of 10 demonstrated an association between the risk of appendicitis and the PM$_{10}$ concentrations at the time of admission (OR, 1.129; 95% CI, 1.016–1.255), 3 days before admission (OR, 1.140; 95% CI, 1.033–1.258), and 7 days before admission (OR, 1.235; 95% CI, 1.087–1.402).

Table 3. Risk of appendicitis associated with increases in the interquartile ranges of particulate matter ≤10 μm in diameter (PM_{10}) in various referent time intervals: a case-crossover analysis

Categories	Time intervals			
	Admission day[*]	3-day moving average[†]	7-day moving average[‡]	14-day moving average[§]
Total	1.027 (0.994–1.060)	1.045 (1.007–1.084)	1.053 (1.005–1.103)	0.938 (0.871–1.009)
Sex				
Male	1.045 (1.001–1.091)	1.076 (1.023–1.132)	1.103 (1.035–1.176)	0.994 (0.897–1.101)
Female	1.003 (0.954–1.054)	1.009 (0.954–1.066)	1.001 (0.935–1.071)	0.883 (0.795–0.981)
Age, yr				
<10	1.129 (1.016–1.255)	1.140 (1.033–1.258)	1.235 (1.087–1.402)	1.042 (0.846–1.282)
10–19	1.013 (0.943–1.089)	1.032 (0.951–1.121)	1.021 (0.919–1.135)	0.897 (0.762–1.056)
20–29	1.013 (0.936–1.096)	1.003 (0.921–1.093)	0.991 (0.891–1.101)	0.839 (0.709–0.993)
30–39	0.998 (0.929–1.072)	1.013 (0.926–1.109)	1.024 (0.914–1.148)	0.900 (0.753–1.075)
40–49	0.985 (0.891–1.088)	1.054 (0.937–1.184)	1.073 (0.936–1.231)	0.940 (0.766–1.153)
50–60	1.063 (0.964–1.171)	1.056 (0.939–1.188)	0.993 (0.859–1.149)	1.053 (0.841–1.319)
≥60	1.069 (0.946–1.207)	1.046 (0.914–1.198)	1.122 (0.955–1.318)	1.111 (0.851–1.149)
Season				
Warm season[∥]	0.865 (0.817–0.916)	0.807 (0.756–0.860)	0.690 (0.637–0.746)	0.420 (0.369–0.478)
Cold season[¶]	1.252 (1.192–1.316)	1.424 (1.343–1.509)	1.716 (1.593–1.849)	2.632 (2.334–2.967)

All models were adjusted for daily mean temperature and humidity.

[*] Current day: PM_{10} exposure level on the day of hospital admission.

[†] PM_{10} exposure level between current hospital admission day and two days before hospital admission (lag 0–2).

[‡] PM_{10} exposure level between current hospital admission day and 6 days before hospital admission (lag 0–6).

[§] PM_{10} exposure level between current hospital admission day and 13 days before hospital admission (lag 0–13).

[∥] The warm season runs from April to September.

[¶] The cold season runs from October to March.

Seasonal differences: The risk of appendicitis during the cold season was significantly associated with the mean PM_{10} concentration at various lag times, including at the time of admission (OR, 1.252; 95% CI, 1.192–1.316), three days prior (OR, 1.424; 95% CI, 1.343–1.509), seven days prior (OR, 1.716; 95% CI, 1.593–1.849), and 14 days prior (OR, 2.632; 95% CI, 2.334–2.967). Conversely, no significant association was found between PM_{10} concentration and increased appendicitis risk during the warm season.

Fig. 2 depicts the risk of appendicitis across various reference time intervals, highlighting the associated interquartile ranges of PM_{10} through case-crossover analysis. This analysis includes data from the total patient population, patients aged 0–9, males, and those observed during the cold season over various exposure time intervals. The risk of appendicitis was linked to PM_{10} concentrations when the exposure period ranged from 3 to 7 days prior to hospital admission. In subgroup analyses, a significant association was found between the risk of appendicitis and PM_{10} concentrations during an exposure interval of two to nine days for male patients and those under 10 years of age. Additionally, during the cold season, the risk of appendicitis increased as the exposure interval extended from 1 day to 14 days.

The overall risk of appendicitis during the various reference time intervals associated with increases in the interquartile ranges of PM_{10}, stratified by sex, season, and age are shown in Tables 4, 5. In males, the risk of appendicitis consistently increased over the case period

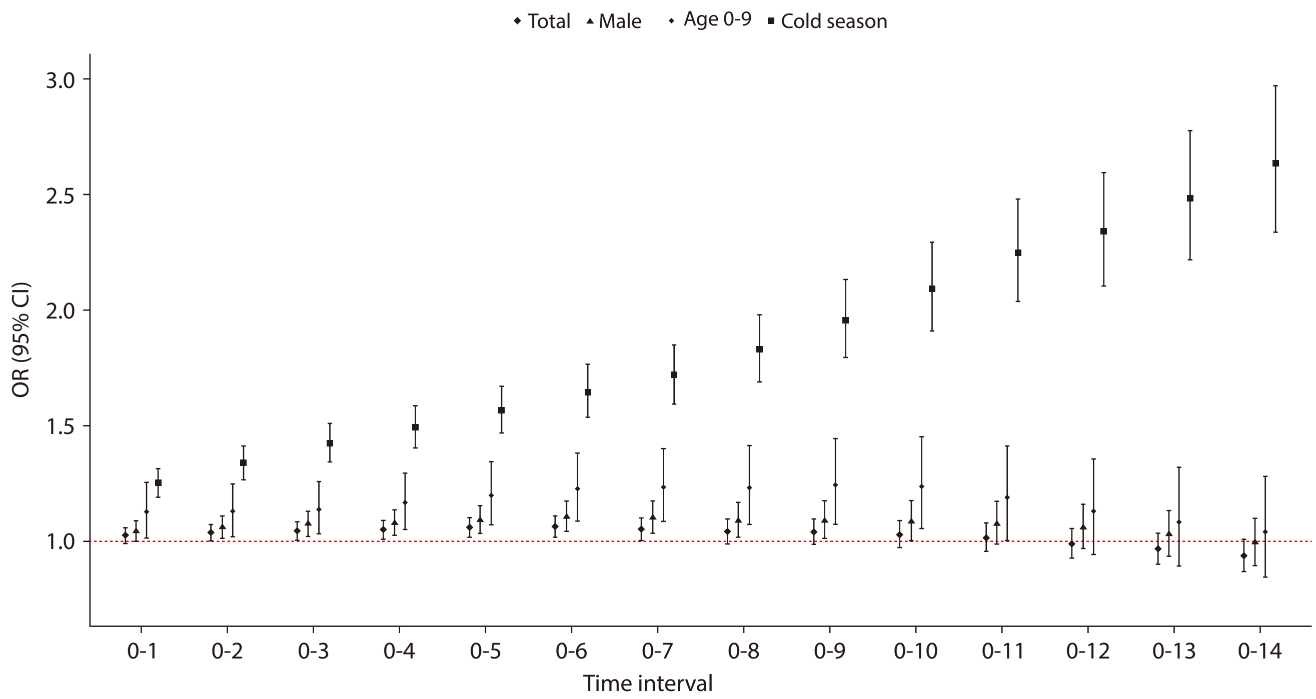

Fig. 2. Risk of appendicitis during various reference time intervals with associated interquartile ranges of PM$_{10}$ using case-crossover analysis, among total patients, patients 0–9 years of age, male patients, and cases that occurred during the cold season. PM$_{10}$, particulate matter ≤10 μm in diameter.

from one to six days. During the cold season, the longer the case period, the higher the risk of appendicitis, with the greatest risk observed at a 14-day interval (OR, 2.632; 95% CI, 2.334–2.967). The correlation between PM$_{10}$ and other air pollutants is summarized in Supplement 3. Since no air pollutant demonstrated a high correlation with PM$_{10}$, no variable was excluded from the two-pollutant model. We observed varying trends in the association between PM$_{10}$ and appendicitis across two-pollutant models. While the association remained statistically significant when adjusted for SO_2, CO, and O_3, it was attenuated upon adjustment for NO_2 (Table 6). Since the AirKorea database began recording PM$_{2.5}$ measurements in 2015, we included a sensitivity analysis to assess the impact of PM$_{2.5}$ on the study results using a two-pollutant model with both PM$_{10}$ and PM$_{2.5}$, detailed in Supplement 4.

Discussion

Key results

The present study suggests that short-term exposure to PM$_{10}$ is significantly associated with an increased risk of appendicitis in boys under the age of 10 who were hospitalized during the cold season. To the best of our knowledge, this study is the first to examine the impacts of PM$_{10}$ exposure on acute appendicitis across diverse subgroups and various lag intervals within the Korean population.

Interpretation

Ewha Womans University Mokdong Hospital, affiliated with Ewha Medical School, serves as the sole community-based tertiary medical institution for a population of 1.5 million in

Table 4. Overall risk of appendicitis during various referent time intervals associated with increases in the interquartile ranges of PM_{10}, stratified by sex and season

Time intervals	Total	Sex		Season	
		Male	Female	Warm season*	Cold season†
0–1	1.027 (0.994–1.060)	1.045 (1.001–1.091)	1.003 (0.954–1.054)	0.865 (0.817–0.916)	1.252 (1.192–1.316)
0–2	1.037 (1.002–1.074)	1.062 (1.014–1.112)	1.007 (0.956–1.061)	0.827 (0.777–0.879)	1.338 (1.268–1.412)
0–3	1.045 (1.007–1.084)	1.076 (1.023–1.132)	1.009 (0.954–1.066)	0.807 (0.756–0.860)	1.424 (1.343–1.509)
0–4	1.051 (1.012–1.091)	1.080 (1.026–1.137)	1.018 (0.963–1.076)	0.800 (0.750–0.854)	1.493 (1.405–1.586)
0–5	1.061 (1.019–1.104)	1.094 (1.036–1.155)	1.024 (0.966–1.086)	0.781 (0.730–0.836)	1.567 (1.469–1.671)
0–6	1.064 (1.020–1.110)	1.107 (1.043–1.174)	1.019 (0.957–1.084)	0.745 (0.693–0.801)	1.647 (1.536–1.765)
0–7	1.053 (1.005–1.103)	1.103 (1.035–1.176)	1.001 (0.935–1.071)	0.690 (0.637–0.746)	1.716 (1.593–1.849)
0–8	1.042 (0.992–1.096)	1.091 (1.018–1.169)	0.991 (0.921–1.066)	0.636 (0.583–0.693)	1.829 (1.688–1.981)
0–9	1.042 (0.987–1.099)	1.092 (1.015–1.176)	0.988 (0.914–1.068)	0.591 (0.538–0.648)	1.956 (1.795–2.131)
0–10	1.031 (0.974–1.092)	1.086 (1.003–1.176)	0.974 (0.897–1.059)	0.552 (0.500–0.611)	2.092 (1.908–2.294)
0–11	1.017 (0.956–1.081)	1.078 (0.990–1.174)	0.956 (0.875–1.044)	0.529 (0.475–0.588)	2.246 (2.034–2.479)
0–12	0.988 (0.926–1.054)	1.061 (0.970–1.161)	0.917 (0.836–1.006)	0.496 (0.443–0.556)	2.335 (2.102–2.594)
0–13	0.966 (0.902–1.035)	1.030 (0.936–1.135)	0.903 (0.818–0.997)	0.462 (0.409–0.522)	2.478 (2.214–2.774)
0–14	0.938 (0.871–1.009)	0.994 (0.897–1.101)	0.883 (0.795–0.981)	0.420 (0.369–0.478)	2.632 (2.334–2.967)

All models were adjusted for daily mean temperature and humidity.

PM_{10} , particulate matter ≤10 μm in diameter.

*The warm season runs from April to September.

†The cold season runs from October to March.

the Yangcheon-gu district of Seoul. Each year, the hospital performs approximately 500 to 600 appendectomies, with the majority of these cases being emergency surgeries for acute appendicitis. Over the 18-year study period, about 72% of the appendicitis patients came from three neighboring administrative districts. In terms of exposure validity, we accessed national air pollution data from AirKorea for analysis. We then correlated this data with our patient records, matching it to the inpatients' home addresses. As for the validity of our outcome definition, all study participants underwent an appendectomy following their diagnosis. This procedure followed a standardized method for critical pathways and was verified by biopsy, ensuring the accuracy and consistency of our outcome definitions.

Regarding sex differences, biological differences, such as variations in immune response and hormonal influences, may make males more susceptible to inflammatory triggers caused by air pollution. Additionally, behavioral factors, including differences in outdoor activities and exposure levels, could contribute to the observed disparity [12].

Children under 10 may be more vulnerable to PM_{10} exposure due to their developing respiratory and immune systems, which are more susceptible to inflammatory agents. Their higher breathing rates relative to body size and increased time spent outdoors can lead to greater exposure to air pollutants. Additionally, because their immune systems are not fully developed, they are less capable of handling environmental insults such as air pollution [13]. Cold weather can exacerbate the effects of PM_{10} on respiratory and immune systems, potentially triggering inflammatory responses more readily [14].

This study observed that seasonal variations in air pollution exposure levels significantly

Table 5. Overall risk of appendicitis during various reference time intervals associated with increases in the interquartile range of PM_{10}, stratified by age groups

Lag days	Age (yr)						
	<10	10–20	20–29	30–39	40–49	50–59	≥60
0–1	1.129 (1.016–1.255)	1.013 (0.943–1.089)	1.013 (0.936–1.096)	0.998 (0.929–1.072)	0.985 (0.891–1.088)	1.063 (0.964–1.171)	1.069 (0.946–1.207)
0–2	1.130 (1.023–1.248)	1.022 (0.949–1.100)	1.022 (0.942–1.109)	1.001 (0.921–1.087)	1.020 (0.915–1.138)	1.066 (0.954–1.190)	1.043 (0.924–1.178)
0–3	1.140 (1.033–1.258)	1.032 (0.951–1.121)	1.003 (0.921–1.093)	1.013 (0.926–1.109)	1.054 (0.937–1.184)	1.056 (0.939–1.188)	1.046 (0.914–1.198)
0–4	1.169 (1.054–1.297)	1.038 (0.953–1.129)	1.008 (0.927–1.095)	1.027 (0.936–1.126)	1.065 (0.944–1.202)	1.034 (0.920–1.162)	1.056 (0.927–1.203)
0–5	1.201 (1.074–1.342)	1.044 (0.955–1.142)	1.012 (0.927–1.106)	1.045 (0.950–1.149)	1.084 (0.955–1.232)	1.017 (0.897–1.152)	1.760 (0.938–1.234)
0–6	1.227 (1.090–1.382)	1.046 (0.948–1.153)	1.016 (0.924–1.118)	1.031 (0.928–1.145)	1.082 (0.954–1.228)	1.005 (0.879–1.148)	1.109 (0.956–1.287)
0–7	1.235 (1.087–1.402)	1.021 (0.919–1.135)	0.991 (0.891–1.101)	1.024 (0.914–1.148)	1.073 (0.936–1.231)	0.993 (0.859–1.149)	1.122 (0.955–1.318)
0–8	1.233 (1.076–1.414)	1.007 (0.899–1.128)	0.972 (0.867–1.090)	1.011 (0.897–1.141)	1.050 (0.908–1.214)	0.997 (0.853–1.165)	1.132 (0.953–1.346)
0–9	1.245 (1.074–1.444)	1.026 (0.908–1.160)	0.964 (0.853–1.090)	0.998 (0.878–1.136)	1.033 (0.886–1.206)	0.982 (0.831–1.160)	1.156 (0.961–1.391)
0–10	1.238 (1.055–1.452)	1.014 (0.890–1.155)	0.947 (0.830–1.080)	0.988 (0.861–1.134)	1.023 (0.869–1.204)	0.979 (0.819–1.170)	1.157 (0.945–1.417)
0–11	1.192 (1.005–1.414)	0.998 (0.869–1.146)	0.915 (0.797–1.050)	0.994 (0.856–1.154)	1.011 (0.848–1.204)	1.003 (0.831–1.211)	1.150 (0.925–1.429)
0–12	1.131 (0.944–1.357)	0.962 (0.831–1.112)	0.879 (0.760–1.017)	0.970 (0.829–1.134)	0.991 (0.823–1.194)	1.031 (0.844–1.259)	1.122 (0.891–1.414)
0–13	1.085 (0.892–1.320)	0.929 (0.795–1.084)	0.866 (0.740–1.013)	0.937 (0.793–1.107)	0.969 (0.798–1.177)	1.058 (0.857–1.308)	1.105 (0.864–1.415)
0–14	1.042 (0.846–1.282)	0.897 (0.762–1.056)	0.839 (0.709–0.993)	0.900 (0.753–1.075)	0.940 (0.766–1.153)	1.053 (0.841–1.319)	1.111 (0.851–1.149)

All models were adjusted for daily mean temperature and humidity.
PM_{10}, particulate matter ≤10 µm in diameter.

impacted the risk of appendicitis. Interestingly, our findings contradict those of previous studies, which suggested that appendicitis incidence was higher in the summer due to increased outdoor activities [15]. Our results lead us to hypothesize that climate factors, such as temperature and humidity, play a more significant role in increasing appendicitis risk than does outdoor activity. Additionally, the distinct weather conditions associated with Korea's four seasons may also influence the results observed in our study.

Our study has several key strengths and novelties. First, it specifically targeted the Korean population. Despite Korea's relatively high air pollution levels compared to Western countries, to our knowledge, this is the first study utilizing Korean data to explore the relationship between PM_{10} and appendicitis. Second, our methodology is distinctive as it aimed to categorize cases across various dimensions, including age, sex, and season. While appendicitis is recognized as an acute condition linked to short-term effects of PM_{10}, the critical exposure period remains unclear. Therefore, diverging from previous research that primarily examined a lag effect of fewer than 3 days, our study investigated the impact of PM_{10} over a 14-day period prior to hospital admission.

Table 6. Risk of appendicitis during various reference time intervals associated with increases in the interquartile range of PM_{10} in the two-pollutant models

Lag	Single mollutant	Two pollutant models			
	PM_{10}	Adjusted SO_2	Adjusted NO_2	Adjusted CO	Adjusted O_3
0–1	1.027 (0.994–1.060)	1.033 (0.995–1.071)	1.005 (0.970–1.042)	1.017 (0.979–1.056)	1.017 (0.979–1.056)
0–2	1.037 (1.002–1.074)	1.041 (1.001–1.082)	1.009 (0.971–1.049)	1.029 (0.988–1.071)	1.029 (0.988–1.071)
0–3	1.045 (1.007–1.084)	1.049 (1.005–1.094)	1.011 (0.970–1.054)	1.035 (0.991–1.081)	1.035 (0.991–1.081)
0–4	1.051 (1.012–1.091)	1.049 (1.005–1.095)	1.018 (0.976–1.061)	1.043 (0.999–1.090)	1.043 (0.999–1.090)
0–5	1.061 (1.019–1.104)	1.058 (1.011–1.108)	1.030 (0.985–1.077)	1.059 (1.011–1.109)	1.059 (1.011–1.109)
0–6	1.064 (1.020–1.110)	1.060 (1.010–1.113)	1.039 (0.991–1.089)	1.067 (1.016–1.120)	1.067 (1.016–1.120)
0–7	1.053 (1.005–1.103)	1.044 (0.990–1.101)	1.032 (0.980–1.086)	1.064 (1.008–1.123)	1.064 (1.008–1.123)
0–8	1.042 (0.992–1.096)	1.029 (0.971–1.090)	1.026 (0.970–1.085)	1.066 (1.006–1.129)	1.066 (1.006–1.129)
0–9	1.042 (0.987–1.099)	1.027 (0.965–1.093)	1.032 (0.972–1.096)	1.077 (1.012–1.147)	1.077 (1.012–1.147)
0–10	1.031 (0.974–1.092)	1.002 (0.938–1.072)	1.020 (0.956–1.088)	1.062 (0.993–1.136)	1.062 (0.993–1.136)
0–11	1.017 (0.956–1.081)	0.995 (0.926–1.069)	1.012 (0.945–1.085)	1.055 (0.981–1.134)	1.055 (0.981–1.134)
0–12	0.988 (0.926–1.054)	0.962 (0.891–1.038)	0.986 (0.916–1.062)	1.029 (0.952–1.111)	1.029 (0.952–1.111)
0–13	0.966 (0.902–1.035)	0.941 (0.868–1.020)	0.975 (0.901–1.055)	1.017 (0.937–1.105)	1.017 (0.937–1.105)
0–14	0.938 (0.871–1.009)	0.913 (0.837–0.996)	0.960 (0.882–1.044)	1.003 (0.918–1.096)	1.003 (0.918–1.096)

All models were adjusted for daily mean temperature and humidity.

PM_{10}, particulate matter ≤10 μm in diameter; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone.

Comparison with previous studies

In Linfen City, China, an increase of 10 μg/m^3 in pollutant levels, considering a 1-day lag, was associated with heightened health risks from January to December 2018. Specifically, the relative risks and their 95% CIs were as follows: PM_{10}: 1.0179 (1.0129–1.0230), SO_2: 1.0236 (1.0184–1.0288), and NO_2: 1.0979 (1.0704–1.1262). The study indicated that men and young adults aged 21–39 years were particularly susceptible to the effects of air pollution. Furthermore, the impact of air pollutants was more pronounced during the colder months, though the seasonal variation was not statistically significant [16]. In Italy, factors predicting perforated appendicitis included consultation delay (OR, 1.621; 95% CI, 1.288–2.039; $P<0.001$) and the 2-day lag mean concentration of PM_{10} (OR, 1.066; 95% CI, 0.007–1.130; $P=0.029$) during the period from January 1 to December 31, 2014 [17]. In Taiwan, when temperatures fell below 23°C, higher levels of PM_{10} were linked to a significant increase in hospital admissions for appendicitis between 2009 and 2013 [7]. In New Zealand, no correlation was found between PM_{10} levels and admissions for appendicitis from January to December 2018 [18]. While the above-mentioned three studies found associations between PM_{10} and appendicitis admissions, other results concerning age and climate varied.

Limitations

Our study has several limitations. First, since nationwide air pollutant data are only available by district, we could not account for variations between smaller regional units. Consequently, we cannot ensure a precise match between the pollution data from our database and the actual pollution levels in the patients' neighborhoods.

Second, we did not take into account the socioeconomic and lifestyle data of the patients; therefore, we did not categorize our patients as outdoor or indoor workers to explore any potential association between outdoor activity and appendicitis. However, it is important to note that appendicitis is an acute condition, and the data were gathered from a single institution located near where most patients reside. We assumed that the levels of air pollution exposure were varied across different neighborhoods. Additionally, the use of a case-crossover data analysis helped to eliminate bias from personal confounders.

Third, since our AirKorea database only began recording $PM_{2.5}$ measurements in 2015, we were unable to assess the effects of $PM_{2.5}$ across all participants. Instead, we conducted a two-pollutant model analysis using PM_{10} and $PM_{2.5}$ data from cases recruited between 2015 and 2018. Our findings indicate that the overall effect size of $PM_{2.5}$ was greater than that of PM_{10}, and it was associated with smaller P-values. Therefore, further studies that focus on $PM_{2.5}$ as the primary exposure are warranted.

Suggestion for further studies

These comprehensive analyses may offer additional insights into preventive measures for appendicitis that are typically overlooked in clinical practice. Further research is essential to enhance our understanding of appendicitis epidemiology and to help decrease the incidence of the condition.

Conclusion

Our study revealed a positive association between PM_{10} concentration and the incidence of appendicitis, suggesting that short-term exposure to PM_{10} may trigger appendicitis. The risk was notably higher in boys under the age of 10 and during the colder seasons. However, these findings should not be interpreted as direct evidence that PM_{10} directly causes appendicitis. To further investigate these relationships, additional ecological and large-scale epidemiological studies are necessary.

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Conflict of interest

Eunhee Ha has been a dean of the Ewha Womans University College of Medicine since August 2021. Ryung-Ah Lee has been an associate editor of the *Ewha Medical Journal* since August 2023. However, they were not involved in the peer review process or decision-making.

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Data availability

Research data and R code is available upon request to the corresponding author. Please contact them for the cooperative studies.

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Supplementary materials

Supplementary materials are available from: https://doi.org/10.12771/emj.2024.e38.

Supplement 1. Distribution of residential areas (administrative districts) of appendicitis (n=6,526)
Supplement 2. Summary statistics for daily air pollutants measured at monitoring stations during the study period of 2001–2018
Supplement 3. Spearman correlation matrix between daily air pollutants during the study period (2001–2018)
Supplement 4. Risk of appendicitis associated with increases in the PM_{10} and $PM_{2.5}$ (study period: 2015-2018)

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