Air Pollution and Respiratory Morbidity in Israel: A Review of Accumulated Empiric Evidence

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ABSTRACT: Studies of the respiratory effects of air pollution in Israel published in peer-reviewed journals have been infrequent. Most empiric evidence relates to the association between air pollution and childhood asthma; other air pollution effects on other illnesses are less thoroughly studied. Our evaluation provides a possible explanation for the quite contradictory results demonstrated in the various studies. Actual effect estimates appear to differ considerably, ranging from no air pollution effect to a reasonably strong association detected between PM_{10} and asthma. We attribute these discrepancies to different research methodologies and different types of data used in various studies.

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The respiratory effects of chronic exposure to ambient air pollution are well established [1-4]. These effects manifest as inflammation of the bronchial airways, and episodes of reversible bronchoconstriction, sputum production, wheezing and asthma [1-11]. Several studies also indicated that exposure to air pollution tends to increase the risk of chronic respiratory symptoms (including asthma) that are associated with decreased life expectancy and may exert a lifelong effect on children's health [1-4].

An increase in asthma prevalence worldwide has been documented in several studies [1-5,10-14]. In the United States, for instance, the number of people diagnosed with asthma increased by 4.3 million between 2001 and 2009, reaching about 8% of the total population in 2009 [15]. Asthma is also a major health concern in Israel, affecting at least 7% of children [16]. According to Shohat et al. [16], the prevalence rate of asthma among 13 to 14 year old boys in Israel stands at about 7.3%, in contrast to 6.7% among girls of the same age. In another study in 17 year old Israel military conscripts for the period 1998–2004, the prevalence of asthma was found to be even higher, reaching 8.6% in male and 6.9% in female recruits [17].

Population studies of respiratory morbidity in Israel do not show a consistent impact of environmental pollution. We attribute such ambiguity to different research methodologies and different types of data used in different studies

In this review we summarize studies published in international peer-reviewed journals that focus on the association between ambient air pollution and respiratory morbidity in Israel. We propose possible explanations for the contradictory results found in some of these studies.

RESPIRATORY MORBIDITY AND AIR POLLUTION IN ISRAEL

The main sources of air pollution in Israel are energy production facilities, transportation, and industry [18,19]. Since these facilities are largely concentrated in the coastal plain, the highest levels of air pollution are detected in these areas [18]. A rapid increase in the number of motor vehicles and rapidly increasing road density have exacerbated air pollution problems throughout the country [18,20]. According to the World Bank [21], the number of vehicles per kilometer of road in Israel stands at 133, compared to 42 vehicles per kilometer in Finland, 37 in France, 31 in Norway, and 38 in the U.S. The effect of anthropogenic sources of air pollution in Israel is also exacerbated by extreme weather events such as dust storms [22], which lead to high concentrations of particulate matter (PM) in the air.

Over the past few decades, several studies have attempted to investigate the effects of air pollutants on respiratory morbidity in Israel [6-10,13,23-26]. However, that research focused mainly on urban areas around Ashkelon in the south [24,26] and Hadera and Haifa in the north [6-8,23]. Most of these studies revealed adverse effects of air pollution on respiratory health, albeit at different levels of statistical significance.

In an early study, using average monthly measurements and half-hour concentrations of NO_x and SO_2, Goren and Hellmann [26] compared Ashdod (considered a highly polluted area) with Hadera (a non-polluted area). Not surprisingly, the study revealed a higher prevalence of reported respiratory symptoms among children in Ashkelon compared to children in Hadera. In particular, the relative risk (RR) for children from Ashkelon to have sputum was as high as 1.47 ($P < 0.05$), cough accompanied by sputum 1.55 ($P < 0.01$), and asthma 2.66 ($P < 0.05$).

In another study, Goren et al. [7] looked into the prevalence rates of respiratory symptoms among schoolchildren exposed to different average levels of NO_x and SO_2 in the Haifa bay area. The study revealed a RR of 1.38 for sputum with cold and 1.81 for sputum without cold for children residing in highly polluted areas compared to children residing in areas with low pollution ($P < 0.01$). However, there was no consistent trend of reduced pulmonary function among children from different residential areas, and all measured values of pulmonary function tests (PFTs) were within the normal range. Asthma prevalence was also not significantly different ($P > 0.5$) in residential areas characterized by different levels of air pollution.

In a follow-up study, Goren and Hellmann [23] evaluated changes in the prevalence rates of asthma among schoolchildren (aged 13–14) during the period 1980–1989. In their study, air pollution levels were determined according to concentrations of SO_2 and NO_x, counted as the total number of air pollution events during which half-hour averages of SO_2 or NO_x were above an arbitrary threshold, set as one-quarter of the local air quality pollution standards (183 mg/m^3 for SO_2 and 235 mg/m^3 for NO_x). During the study period, a significant increase in asthma prevalence occurred among fifth-grade children in all the communities under analysis: odds ratio (OR) 1.79, 95% confidence interval (CI) 1.16–2.74, $P < 0.01$. A significant increase in the prevalence of wheezing, accompanied by shortness of breath, was also observed (OR 1.759, 95%CI 1.11–2.28, $P < 0.05$). However, the authors could not attribute the prevalence of asthma to environmental variables, concluding that the main reason for the increase in asthma and related respiratory symptoms remained unclear.

We suggest that future research judiciously select an appropriate exposure assessment method to determine health effects, the individual exposure estimates being the most preferable exposure assessment tool

In a separate study, Bibi et al. [9] evaluated the interaction effect between SO_2 and NO_x and meteorological conditions in Ashkelon – measured by ambient temperature, relative humidity and barometric pressure – on the number of emergency room (ER) visits due to respiratory symptoms (asthma and cough). Air pollution levels and meteorological data were represented by peak values observed within 24 hours prior to the ER admittance and by the average values of air pollution during the week before the ER admittance. The authors concluded that 24 hour peak levels and 7 day averages of SO_2 and NO_x reported prior to ER visits helped to predict, with a sufficient degree of accuracy, approximately 12%, the daily number of ER visits linked to respiratory morbidity.

In another study Garty and team [13] investigated the association between air pollutants (NO_2, SO_2, O_3) and the number of ER visits of asthmatic children in the Tel Aviv area in 1995. A positive association (measured by the Pearson correlation coefficient) was found between the number of ER visits due to asthma outbreaks in children and their exposure to SO_2 ($r = 0.60$) and NO_2 ($r = 0.68$). However, the correlation between the number of ER visits and PM_{10} levels was relatively low ($r = 0.32$), while the number of ER visits by asthmatic children showed a negative correlation with observed O_3 levels ($r = -0.61$).

In a more recent study, Dubnov et al. [6] used geographic information system (GIS) tools to analyze individual (child-specific) estimates of long-term exposure to air pollution and its association with children's lung function development. The average levels of air pollutants and interaction between NO_2 and SO_2, measured as a sum of acute air pollution events, were analyzed for different residential areas neighboring a major coal-fired power station in the Hadera region. The researchers found a negative association between the estimated levels of exposure of individuals and changes in the forced expiratory volume in the first second (FEV1), showing a decline of up to 10.2% for the most polluted area compared to the least polluted one; similar results were also seen for forced vital capacity (FVC). The results concluded that air pollution from a coal-fired power station, although not exceeding local air pollution standards, had a negative effect on the development of children's lung function. The study did not include other pollutants, such as PM_{10} and $PM_{2.5}$, due to the limited number of PM monitoring stations in the study area.

In a follow-up study in the same region (Hadera, Pardes Hanna, Karkur), Yogev-Baggio and colleagues [10] evaluated the effects of exposure to air pollution by NO_x and SO_2 on the development of pulmonary function in children, characterized by different respiratory health status. The exposure levels were evaluated individually for each child in the sample using GIS tools. The study demonstrated a higher prevalence of respiratory symptoms among children growing up in polluted areas compared to children residing in low pollution areas. In particular, a decrease in FEV1 of about 19.6% for children with chest symptoms ($P < 0.001$), 11.8% for healthy children ($P < 0.001$), and approximately 7.9% for children diagnosed with asthma ($P > 0.2$) was found. In other words, exposure to air pollution had the greatest effect on children with chest symptoms. The authors explained this phenomenon as follows: this untreated symptomatic group might experience the most severe injury of their respiratory system as a result of exposure to ambient air pollution, which is reflected by a reduction in their FEV1 and FVC values, while children with asthma were less affected by air pollution as they have lower baseline FEV1 and FVC values, slower growth rates, and are treated with anti-asthma drugs. As a result, PFT changes in asthmatic children may be affected less by exposure to air pollution.

In a separate study, Portnov et al. [8] analyzed whether the high prevalence of childhood asthma (6 to 14 years old) in northern Israel is linked to air pollution. Individual exposure to ambient levels of SO_2 and PM_{10} for each child in the sample was estimated using GIS tools and Bayesian modeling. The analysis revealed that childhood asthma in the Haifa bay area is associated with PM_{10} exposure (OR 1.11, 95%CI 1.05–1.17, $P < 0.01$); however, no significant association was found between SO_2 level and asthma prevalence ($P > 0.2$) when PM_{10} and SO_2 were simultaneously introduced into the models. Based on these results, the authors concluded that exposure to airborne PM_{10}, even at relatively low concentrations (40–50 mg/m^3), being below international air pollution standards (55–70 mg/m^3), appears to be a significant risk factor for childhood asthma in urban areas.

Fireman and colleagues [27] evaluated lung inflammation resulting from exposure to airborne particulate matter (PM). The researchers used the induced sputum (IS) technology to monitor PM concentrations biologically in the lungs of asthmatic children. They concluded that PM is a significant risk factor for eosinophilic inflammation due to higher levels of exhaled nitric oxide in the eosinophilic group than in the non-eosinophilic group. In particular, children whose lungs and airways displayed high concentrations of $PM_{2.5}$ exhibited the highest risk of eosinophilic inflammation (OR 10.7, 95%CI 2.052–56.400, $P < 0.01$).

In a separate case-control study, Nirel et al. [19] examined whether hospitalization of children due to respiratory diseases in Jerusalem is related to residential exposure to traffic-related air pollution. The study focused on 0–14 year old children hospitalized between 2000 and 2006. Individual measures of exposure included distance from the place of residence to the nearest main road, the total length of the main road, traffic volume, and the bus load within buffers of 50, 150, and 300 meters of each address. The study revealed that children whose homes were within 50 m from bus traffic exhibited increased odds of respiratory hospitalization (OR 1.16, 95%CI 1.04–1.30, $P < 0.01$).

A summary of air pollution effects on respiratory morbidity in different studies in Israel is shown in Tables 1 and 2. In particular, Table 1 depicts the different parameters examined in the various studies and the degree of association of air pollution exposure and respiratory morbidity. Concurrently, Table 2 provides a brief summary of studies examining the effect of air pollution on respiratory morbidity in Israel.

As Tables 1 and 2 demonstrate, most studies investigating the association between air pollution and respiratory morbidity in Israel were conducted before 2000 and focused primarily on Hadera, Ashkelon and Haifa. Most of these studies were based on questionnaires filled in by the children's parents [7,23-26,28,29]. Characteristically, these studies did not detect any significant air pollution/respiratory morbidity association, apparently because patient-reported outcomes might result in a reporting bias [7,23-25,28,29]. Concurrently, studies based on a physician's diagnosis observed a significantly negative effect

Table 1. Classification attributes of studies focusing on the association between air pollution and respiratory morbidity in Israel

Author (year) [ref]	Air pollutants association with respiratory morbidity			Study area			Individual exposure	Asthma	Diagnosis by a physician	General respiratory morbidity	Lung function	Study period	
	PM	NO_x	SO_2	South	North	Center						Before 2000	After 2000
A. Studies showing a statically significant effect of air pollution on respiratory morbidity, including asthma													
Bibi et al. (2002) [9]	-	+	+	√				+	√			+	
Garty et al. (2009) [13]		+	+			√		+	√			+	
Goren and Hellmann (1988) [26]		+	+	√	√			+		+		+	
Dubnov et al. (2007) [6]		+	+		√		+		√		+	+	
Portnov et al. (2011) [8]	+		-		√		+	+	√				+
Yogev-Baggio et al. (2010) [10]		+*	+*		√		+		√	+	~*	+	
Fireman et al. (2014) [27]	+					√	+	+	√	+	+		+
B. Studies showing only weak or statistically insignificant effects of air pollution on respiratory morbidity, including asthma													
Goren et al. (1988) [28]		°	°	√				-		°	-	+	
Goren et al. (1990) [7]			°		√			~		~	-	+	
Goren et al. (1991) [29]		-	-		√			~		~	~	+	
Goren and Hellmann (1997) [23]		-	-		√			+		~	~	+	
Goren et al. (1999) [31]	°			√				-		-	-	+	
Peled et al. (2001) [24]		-	-	√							~	+	
Peled et al. (2005) [25]	°			√							~	+	

+ = Statistically significant association; - = No significant association; ° = Positive association for some symptoms; * = Positive association among some population groups; ~ = Positive association in some regions/communities; Blank = No association tested; √ = Covered by the study

Table 2. Brief summary of studies that examined the effect of air pollution on respiratory morbidity in Israel

Author (year) [ref]	Contingent, spatial resolution and time span	Environmental factors and exposure assessment methods	Dependent variable(s)	Diagnosis method	Covariate(s)	Main findings
Bibi et al. (2002) [9]	1020 records of residents of Ashkelon collected in 1992–1995	Regional daily averages of SO_2, NOx, temperature, humidity and barometric pressure	Number of ED visits due to asthma, COPD and chronic bronchitis	Diagnosis by a physician	Age, gender and residential location	The model predicted the number of ED visits with an average estimate error of 12%
Dubnov et al. (2007) [6]	1492 schoolchildren in 2nd and 5th grades living in vicinity of the Orot Rabin coal-fired power station in northern Israel, surveyed consequently in 1996 and 1999	Accumulated numbers of "air pollution events" for SO_2 and NOx exceeding local reference levels; proximity of child's residence to the nearest freeway or a major road	PFT: FVC, FEV1, adjusted for age group and gender	Spirometry measurements by technician, and questionnaires filled in by the children's parents	Height, etc., presence of asthma and chronic bronchitis, housing conditions, parental education, environmental tobacco smoking	FEV1 decline of up to 10.2% observed in children residing in the most polluted areas; similar results for FVC
Garty et al. (2009) [13]	2431 children aged 1–18 years who visited the pediatric ED in the Tel Aviv metropolitan area in 1995	Regional daily averages of SO_2, NO_x, O_3 and PM	Number of ED visits due to acute asthma	Asthma diagnosed by a physician	Month of the visit	The number of ED visits by asthmatic children showed a negative correlation with O_3 levels (r = -0.70), and positive correlations with NO_2 (r = 0.60) and SO_2 (r = 0.68)
Goren and Hellman (1988) [26]	1984 and 1826 schoolchildren in the 2nd and 5th grades living in Hadera and Ashdod, and surveyed in 1980 and 1982, respectively	Regional monthly averages and half-hour concentrations of SO_2 and NO_x	Prevalence of RS and asthma	Questionnaires filled in by the children's parents	SES, household heating by fuel, smoking habits of parents, respiratory diseases in the family	High prevalence of RS (RR = 1.47–2.3, P = 0.002–0.049) and asthma (RR = 2.66, P = 0.039) among children growing up in polluted areas, as compared to children residing in non-polluted areas
Goren et al. (1988) [28]	2303 schoolchildren aged 6–18 years and 3437 adults aged 20–65, residing near power plants, oil refineries and industrial areas of Hevel Yavne and Hof Ashkelon, surveyed in 1984	Regional monthly averages and half-hour concentrations of SO_2 and NOx	RS, asthma, PFT: FVC, FEV1, FEV1/ FVC, PEF, FEV50, and FEV75	Spirometry measurements performed by a technician, and questionnaires filled in by the children's parents	SES, country of origin, household fuel consumption, smoking habits of parents, occupational exposure, respiratory diseases in the family	High prevalence of RS (RR = 2.13–3.89) and asthma (19.5% vs. 15%, P = 0.377) among children growing up in the most polluted area as compared to the least polluted areas. Lower PFT among children residing in the most polluted area (P = 0.054); similar trends seen for adults
Goren et al. (1990) [7]	4334 schoolchildren in the 2nd and 5th grades living in the Haifa bay area, and surveyed in 1984	Regional monthly averages and half-hour concentrations of SO_2	RS, asthma, PFT: FVC, FEV1, FEV1/ FVC, PEF, FEV50, FEV75	As above	Crowdedness index, smoking habits of parents, respiratory diseases in the family, father's country of origin	Higher prevalence of RS among children growing up in medium and high polluted area as compared to low polluted areas (RR = 1.38–1.81); PFT within the normal range
Goren et al. (1991) [29]	915 and 885 schoolchildren in the 2nd and 5th grades living in Hadera, within a 19 km radius of a power plant, and surveyed in 1980 and 1986	Regional monthly averages of SO_2 and NO_x	RS, asthma, PFT: FVC, FEV1, FEV1/ FVC, PEF. Adjusted for children's height	As above	Height, SES, parental smoking	Increased prevalence of RS among 2nd grade children; annual increase in PFT higher in polluted communities compared with less polluted areas
Goren and Hellman (1997) [23]	834, 957, 1074 and 802 schoolchildren in the 2nd, 5th and 8th grades, residing near the power plant in Hadera, and surveyed in 1980, 1983, 1986 and 1989	Regional averages of half-hour air pollution events of SO_2, NO_x and CO	RS, asthma, PFT: FVC, FEV1, FEV1/ FVC	As above	SES, parental smoking	Significant increase in RS prevalence ($P < 0.0018$) and asthma ($P < 0.0005$) among 5th grade children; PFT lower among children with reported asthma
Goren et al. (1999) [31]	976 schoolchildren aged 7–13 living in Beit Shemesh, and surveyed in 1995	24 hour values and daily averages of TSP and PM_{10}	RS, asthma, PFT: FVC, FEV1, FEV1/ FVC, PEF, FEV50, FEV25	As above	SES, crowding index, smoking habits and respiratory diseases of parents, residential heating	Higher prevalence of most RS and asthma among children growing up in a community bordering on the industrial zone; no consistent trend of reduced PFT and PEF among children who live in polluted areas ($P > 0.23$)
Fireman et al. (2014) [27]	136 schoolchildren aged 12.6 ± 2.9 and residing in the Tel Aviv metropolitan area	Regional 3 day averages of PM_{10}, recorded prior to the medical examination	PFT: FEV1/FVC, FEV1, FEV25-75%, FeNO, IS, PM in the IS samples, eoisonophils, and HO-1 enzyme	Asthma diagnosed by a physician; spirometry measurements performed by a technician, and questionnaires filled in by the children's parents	Age, gender, exposure to environmental smoking	The eoisonophilic group displayed higher levels of exhaled NO compared to the non-eoisonophilic group (P < 0.01). Children with more than 80% of $PM_{2.5}$, out of total PM accumulated in the airways, displayed the highest risk of eosinophilic inflammation (OR = 10.7 (95%CI 2.052–56.4, $P < 0.01$). HO-1 enzyme levels in IS also found to correlate positively with % eoisonophils and with $PM_{2\text{-}3}$ µm

PM = particulate matter, ERF = environmental risk factor(s), ED = Emergency Department visit, COPD = chronic obstructive pulmonary disease, SES = socioeconomic status, BMI = body mass index, RR = relative risk, OR = odds ratio, 95%CI = 95% confidence interval, r = Pearson correlation, RS = respiratory symptoms, PFT = pulmonary function test, PEF = expiratory peak flow, FEF50–75 = forced expiratory flow of 50–75%, TSP = total suspended particles, IS = induced sputum, ETS = exposure to tobacco smoking

Table 2. continuation

Author (year) [ref]	Contingent, spatial resolution and time span	Environmental factors and exposure assessment methods	Dependent variable(s)	Diagnosis method	Covariate(s)	Main findings
Peled et al. (2001) [24]	1613, 2445, and 4346 schoolchildren of the 2nd, 5th and 8th grades residing in the Ashkelon District, and surveyed in 1990, 1994 and 1997	Regional averages of SO, and NOx	PFT, FVC, FEV1	Spirometry measurements performed by a technician	Age, SES, BMI, gender, passive smoking, foreign birth	No clear association between PFT and air pollution
Peled et al. (2005) [25]	285 second and fifth grade children living in the Ashkelon district, in proximity to a power plant, oil refineries, and industrial areas, surveyed in 1999	Regional daily averages of $PM_{2.5}$ and PM_{10}	PEF	Self-test of PEF before and after inhaling the bronchodilator	Gender, age, BMI, housing density, severity of illness, parental education and smoking habits, place of birth, temperature, barometric pressure	Significant effect of PM on PEF in Ashdod ($PPM_{2.5} < 0.001$ and Sderot ($PPM_{10} < 0.001$) but not in Ashkelon ($PPM_{2.5} = 0.235$)
Portnov et al. (2011) [8]	3922 schoolchildren in 1st through 8th grade, residing in the greater Haifa metropolitan area and surveyed in 2008–2009	Individual exposure estimates of SO_2 and PM_{10}	Prevalence of asthma	Asthma diagnosed by a physician	Gender, age, SES, city residence, road distance	Asthma prevalence associated with PM_{10} (OR 1.106–1.149, depending on the model) but not with SO_2
Yogev-Baggio et al. (2010) [10]	1182 schoolchildren in 2nd and 5th grades residing near the major coal-fired power plant in the Hadera district, and surveyed in 1996 and 1999	Individual estimates of accumulated air pollution events of SO_2 and NOx	FVC and FEV1	Spirometry measurements and questionnaires filled in by the children's parents; asthma diagnosed by a physician	Height, weight, ETS, asthma, chronic bronchitis, housing conditions, parental education, time lived in the area	Decrease in FEV1 associated with SO_2, NO_x higher in children with chest symptoms ($F = 11.33$, $P < 0.001$) and in healthy children ($F = 10.16$, $P < 0.001$) than in children with asthma ($F = 1.48$, $P = 0.229$)

PM = particulate matter, ERF = environmental risk factor(s), ED = Emergency Department visit, COPD = chronic obstructive pulmonary disease, SES = socioeconomic status, BMI = body mass index, RR = relative risk, OR = odds ratio, 95%CI = 95% confidence interval, *r* = Pearson correlation, RS = respiratory symptoms, PFT = pulmonary function test, PEF = expiratory peak flow, FEF50–75 = forced expiratory flow of 50–75%, TSP = total suspended particles, IS = induced sputum, ETS = exposure to tobacco smoking

of environmental pollution on respiratory morbidity in most cases [8-9,13].

In general, the studies cited in Tables 1 and 2 used two different methods of exposure assessment: individual exposure estimates [6,8,10] and/or zonal estimates [7,9,13,23-28]. Overall, the studies using the individual exposure estimate method [6,8,10] found a significant association between air pollution and chronic respiratory morbidity, whereas studies using zonal estimates (i.e., studies based on the average levels of exposure estimated for whole geographic areas such as census areas) found acute effects of air pollution for visits to the emergency department only and revealed no such effects for other types of respiratory morbidity [7,9,13,23-26,28,29]. Statistically significant effects of air pollutants on respiratory morbidity were also found mostly for SO_2 and NO_x [6,9,13,26] and less so for PM [8,25,30]. However, considering that the studies investigating the PM effect on respiratory and asthma morbidity were only sporadic, the inconclusiveness of their results should be treated with caution.

CONCLUSIONS

The studies summarized in this article do not show a consistent and uniform impact of environmental air pollution on either asthma prevalence or other forms of respiratory morbidity in Israel. In our view, the ambiguity of these results may be reduced in future studies by the use of certain research tools and methodologies. For instance, future research should be based on a physician's diagnoses and should avoid, as much as possible, the collection of medical data via questionnaires. Lastly, there appears to be no consensus among the researchers about methods for assessing environmental exposure or a predefined protocol for evaluating the exposure to air pollution. In particular, our findings suggest that individual exposure assessment may provide better estimates than zonal assessment of exposure, where identical values of air pollution exposure are assigned to all residents of relatively large geographic areas. To examine the impact of air pollution on respiratory health, it is important that the analysis be conducted simultaneously in different regions of the country to confirm the generality of the findings, and that both single and multiple-pollutant models be analyzed, given that different air pollutants may have a combined effect on respiratory morbidity.

As a result, different research findings reported by different studies may be related to non-uniform methods used by researchers, highlighting the importance of developing a standard evaluation methodology for exposure assessment and for determining the effects of air pollution on respiratory morbidity as well as on the prevalence of other diseases that may be caused (or aggravated) by air pollution exposure.

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