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Relationship of ambient air pollutants and hazardous household factors with birth weight among Bedouin-Arabs☆

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HIGHLIGHTS

- We enrolled 959 Bedouin-Arab pregnant women at a hospital in Israel at delivery.
- Exposure to higher temperature and Ozone were associated with lower birth weight.
- The contribution of poor household environment to birth weight reduction was higher.

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ABSTRACT

Background: Air pollution and meteorology exposures during pregnancy have been suggested to be associated with Birth Weight (BW). Yet, the individual medical background and close household environment is rarely addressed. We aimed to evaluate the independent association of BW with meteorological and air pollution exposures during pregnancy, in addition to individual, parental and household risk factors, among the Bedouin-Arab population in Southern Israel; a semi nomadic population, featured by low socio-economic levels and poor housing and household environment.

Methods: In a retrospective cohort study we enrolled pregnant women upon their arrival in the local hospital for delivery during December 2011–April 2013. We interviewed the women and collected data on socio-demographic characteristics, medical history and household environmental hazards. Air pollution (NO_2, SO_2, CO, Ozone and Particulate Matter <2.5 μ and 10 μ in diameter) and meteorological data (temperature, relative humidity), retrieved from 13 monitoring sites, were linked to each woman based on the proximity of her residential address.

Results: A total of 959 women were eligible for the study, half of them resided in temporary tribal localities. Ozone IQR elevation in the 3rd trimester was associated with 0.119 gr decrease in BW (95%CI −0.127 gr; −0.112 gr); temperature IQR elevation in the 3rd trimester was associated with 0.002 gr (95% CI −0.004 gr; −0.001 gr) decrease in BW. Waste in the house surroundings was associated with a decrease of 117.27 gr in BW (95%CI −209.19 gr; −25.34 gr).

Conclusion: Although exposure to high levels of temperature and O_3 were associated with lower BW, the contribution of poor household environment indicators to BW reduction was substantially higher.

1. Introduction

Birth weight (BW) is a key indicator of newborns health and an important determinant of perinatal morbidity and mortality

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(Goldenberg and Culhane, 2007). Low birth weight (LBW), in particular, defined as birth weight less than 2500 gr, is a known risk factor for neurological and developmental adverse outcomes (Taylor et al., 2000; Saigal et al., 2003; Hack et al., 2002). The health care costs of treating newborns with low birth weight, which can rich $13.4 billion annually, is alarming in light of the growing prevalence of this condition (Simmons et al., 2010). Prevalence of low birth weight in Israel was approximately 8.2% in 2008 (Ministry of Health: Birth, 2008) and in the range between 9% and 13% among the Bedouin-Arab population residing in the southern part of Israel (Abu-Ghanem et al., 2012).

Among other factors, BW was found to be associated with exposure to meteorological parameters. Despite significant links between the season at birth (Beltran et al., 2014), high air temperature (Strand et al., 2011; Kloog et al., 2015) and BW described in literature, the underlying biological mechanism of these associations remains unclear (Proietti et al., 2013). One potential explanation involves the placental reaction to high temperatures during pregnancy (Wells, 2002).

In addition to these meteorological parameters, higher levels of air pollution were also reported to be associated with lower birth weight (Ha et al., 2001; Kloog et al., 2012)). The air pollution-induced oxidative stress may have an adverse impact on intrauterine growth, explained by the impaired transport of oxygen and nutrient to the fetus (Schlesinger et al., 2006; Kannan et al., 2006).

When investigating the environmental effects on birth weight it is difficult to differentiate the effect of the meteorological factors from the effect of air pollution effect. The variability in the ozone concentrations, in particular, has been reported to be influenced by meteorological conditions (Lavee et al., 2015).

Numerous studies have investigated the link between air pollution exposure and BW and the results are conflicted (Proietti et al., 2013; Chen et al., 2002; Sram et al., 2005; Geer et al., 1995; Morello-Frosch et al., 2010; Stieb et al., 2012; Gouveia et al., 2004; Dugandzic et al., 2006; Lin et al., 2004; Rogers et al., 2000; Salam et al., 2005). For instance, Geer et al., found a significant decrease in BW, associated with an Inter Quartile Range (IQR) increase in Ozone (O_3) levels during gestational period (Geer et al., 1995). Ha et al., on the other hand, reported a positive association between O_3 exposure on LBW (Ha et al., 2014). Both of the aforementioned studies were performed in areas with relatively high temperatures, the later however was adjusted for season of conception but not for the possible effect of temperature.

There is no consensus on the impact of exposure to extreme temperature during pregnancy on BW (Lawlor et al., 2005; Deschenes et al., 2009; Flouris et al., 2009; Elter et al., 2004; Murray et al., 2000) (Beltran et al., 2014). Although pregnant women were identified as more susceptible to temperature changes during gestation, no direct link was found between heat exposure and adverse birth outcomes (Strand et al., 2011).

To add to the major uncertainty regarding the pathway of meteorological factors and pollutants' emissions on BW, the environmental exposures in the household surroundings of a pregnant woman (such as noise, indoor pollution and waste) are rarely incorporated into the environmental research analysis. The household factors surrounding a woman during gestation might have a tremendous impact on the birth outcome, as it has been shown in general population of developing countries by Bruce et al., in 2000 (Bruce et al., 2000; Boy et al., 2002).

The current study was performed in the Northern Negev— a semi-arid region featured by relatively high temperatures and frequently subjected to dust storms (Krasnov et al., 2014). We investigated the population of Bedouin-Arab origin residing in the area, characterized by low Socio Economic Status (SES) (Central bureau of statistics, 2008) and high exposure to poor household environmental risk factors (Sarov et al., 2008). Uncontrolled use of pesticides around the house, burnings of household waste and raising animals in the house surroundings are frequent in the Bedouin-Arab population. This population resides either in permanent settlements or in temporary shacks or tents and the temporary localities have limited access to municipal infrastructure (Sarov et al., 2008). Previous studies performed in this region found the Bedouin population to be susceptible to air pollution related health outcomes (Sarov et al., 2008; Kordysh et al., 2005; Yitshak-Sade et al., 2014; Karakis et al., 2014), the Bedouin community, therefore, represents an important target population for public health professionals for investigation of the impact of pollution on health.

We aimed to evaluate an independent impact of meteorological and air pollution exposures during pregnancy on BW, beyond the individual, parental and household environment risk factors.

2. Methods

2.1. Study design and definitions

We enrolled women of Bedouin-Arab origin upon their arrival in the Obstetric Emergency Department (OED) of the Soroka University Medical Center (SUMC) for delivery during December 2011–April 2013. SUMC is the only hospital in the area, providing tertiary services to the entire population in the northern Negev (southern Israel) and treating approximately 15,000 of births annually.

Arabic-speaking interviewers recruited the women in the OED during the day shift on working days. All Bedouin women entered the OED in these hours were approached and received a detailed information explaining the study aims and inviting to participate in the study. All the study participants singed an informed consent form before enrollment.

After the delivery, we interviewed the women and collected data on socio-demographic characteristics, family and personal medical history, parental exposure to environmental or occupational hazards, health behavior and maternal diagnoses during pregnancy. The objective medical information on the index delivery was obtained from the Admission-Discharge-Transfer database of the hospital.

The primary outcome was the newborns BW. Newborns that are born at SUMC are routinely weighted immediately after birth using a digital weight. In addition, we retrieved the data on the lack of prenatal care (LOPC), maternal age, preterm delivery, pregnancy age, maternal diabetes and other clinical characteristics. All the maternal characteristics were retrieved from the computerized database of SUMC. Information regarding birthdate is linked to the database through the Ministry of Interior database. LOPC definition is based on the woman's personal report. In the arrival to the obstetric emergency room, each woman is asked regarding prenatal care and asked to present relevant documentations. We treated LOPC as a proxy for socio-economic status.

Since diabetes is frequently under diagnosed we used blood test results and antidiabetic medications purchases (data was available between 2003 and 2013) to identify women with abnormal glucose levels, in addition to confirmed diagnosis. Women were characterized with abnormal glucose levels in the presence of one of the following: (a) at least two fasting blood glucose higher than 100 mg/dL; (b) at least two Hemoglobin A1c tests higher than 5.7% (American Diabetes Asoociation, 2014); (c) confirmed diagnoses of diabetes; (d) the purchase of antidiabetic medication.

2.2. Ethical approval

The study has been reviewed and approved by the local institutional ethics committee of SUMC in accordance with the principles of the Declaration of Helsinki (#5017).

2.3. Study population

All Mothers of Bedouin origin who resided in the area were eligible for the study. Only singleton pregnancies to mothers older than 18 years of age were included in the analysis. We excluded deliveries in the presence of one of the following: (a) gestational age at birth <37 weeks; (b) neonatal BW < 500 g; and if (c) delivery took place out of the hospital. Women with no monitoring site within a radius of 20 km were excluded from the analysis.

2.4. Environmental data

The questionnaire administered after delivery inquired on parental exposure to disturbing environmental hazards (yes/no questions) during the pregnancy period: smell, transportation, sewage, waste, dust and noise; and household hazardous practices (yes/no questions): pesticides and fertilizers use, the use of open fire for cooking and heating and the use of electronic, central or stove for heating.

2.5. Ambient air pollution

Air pollution data - Nitrogen Dioxide [NO_2], Sulfur Dioxide [SO_2], Carbon Monoxide [CO], Ozone [O_3], Particulate Matter <2.5 μ in diameter [$PM_{2.5}$] and <10 μ in diameter [PM_{10}]) and meteorological data (temperature and relative humidity) - were retrieved from 13 monitoring sites located in the area, which sample the air in 5 min intervals. PM_{10}, $PM_{2.5}$ and CO measurements were available only at one monitoring site; NO_2 and SO_2 were available at 13 monitoring sites, O_3, temperature and relative humidity were available at 5, 7 and 2 monitoring sites, respectively. These sites are operated by the Israel Ministry of Environmental protection, the electric company or the local Industrial park Neot-Hovav located 12 km from the largest city in the area.

As 51% of the women reside in small localities or temporary settlements, exact home address geocoding was unavailable. Therefore, for the entire study population, we linked the women's home addresses to the center of their residing locality (at a maximal radius of 10 km), which represented the coordinates for pollution assessment. Air pollution and meteorological exposures were assigned to each woman based on the proximity of her residential locality to the monitoring sites in the area.

We used ArcInfo 10.2 (ESRI, Redlands, CA, USA) to calculate the distance between the addresses and the monitoring stations. Daily average pollutants concentrations were interpolated to all localities using the method of inverse distance weighting, in which every address was assigned a weighted average of the observed values in all available monitoring sites within 20 km radius (Hwang and Jaakkola, 2008; Fisher, 1993): The weights of the pollutants' concentrations were expressed by a function decreasing with distance to the monitoring station from the participant's residence ($w = 1/distance^p$, where $p > 2$, as mostly commonly used in this field).

2.6. Statistical analysis

Continuous variables were compared using *t*-test and are presented as mean ± standard deviation (SD). Categorical variables were compared using Chi Square test and are presented as proportions. Correlations were measured using Spearman correlation test.

We used Generalized Estimation Equation (GEE) models with identity link function to model the association of the time varying environmental exposures and BW, accounting for the cluster of repeated exposures of each woman. Models were adjusted for the type of locality (permanent vs. temporary housing), gestational age at birth, the newborn gender and maternal glycemic status. We observed statistical interaction between ozone and temperature, and therefore included an interaction term in the model as well.

Ambient air pollution exposure was tested as repeated measures of the pollutants' daily averages, with three potential exposure periods defined as (1) the entire pregnancy, (2) the third trimester and (3) the last month of pregnancy. Our choice of exposure windows was a-priory defined based on exposure windows reported in other studies (Strand et al., 2011). We than compared the results obtained from the three models.

P value < 0.05 was considered significant. We used EpiData software to record the questionnaire information and SAS 9.4 package (SAS Institute) for the analysis.

3. Results

About 98% of the women who were invited to participate gave their consent to participation in the study. We enrolled 1823 women, of whom we excluded 117 preterm births and 747 women residing further than 20 km from a monitoring station (Fig. 1). A total of 959 women were defined eligible for study. Participants were 28 years old on average and 9.2% of them had at least one chronic condition (Table 1). About half of the women resided in temporary localities. Women who were excluded from the study were slightly younger (27 years on average, $p = 0.003$). The rates of LOPC ($P = 0.572$), diabetes ($p = 0.913$), hypertension ($p = 0.643$), repeated abortions ($p = 0.907$) and infertility treatment ($p = 0.223$) were similar among women included and excluded from the study.

Of all environmental disturbances women complained mostly about dust, sewage and car-related pollution close to their house. The use of open fire for cooking was highly prevalent, and more frequent among women who resided in temporary localities (Table 2).

Air pollutants concentrations during the study period were as follows [IQR (Median)]: $PM_{2.5}$ 5.3 (3.45) μg/m^3; PM_{10} 47.2 (38) μg/m^3; CO 11.5 (11.5) μg/m^3, SO_2 1.36 (1.31) μg/m^3, NO_2 13.19 (8.08) μg/m^{3}and O_3 22.14 (21.56) μg/m^3. The climate was relatively hot and dry with a daily average temperature of 17.8 °C, reaching a maximal average temperature of 32.3 °C. Daily O_3 average concentrations were higher during the warm seasons (Supplementary Table 1).

Air pollution and meteorological factors were not highly correlated, with the highest correlation estimate observed for temperature and O3 ($rho = -0.54$, $p < 0.01$), besides the evident correlation observed for $PM_{2.5}$ and PM_{10} ($rho = 0.66$, $p < 0.01$), and lowest correlation observed for CO and temperature ($rho = 0.009$, $p < 0.01$) (Supplementary Table 2).

The average newborns' weight was 3262 gr ± 462 gr and 3.9% ($n = 38$) weighted under 2500 gr. The average weights were similar across seasons of birth ($p = 0.202$). Reduction in BW was independently associated with increases of O_3 and temperature concentrations in the 3rd trimester and the last month of pregnancy, but the effects were low. We found a statistical but clinically negligible interaction between temperature and O_3, whereas both factors decreased the BW, and their interaction term adjusted the multiplicative effect of the main effects towards higher values of

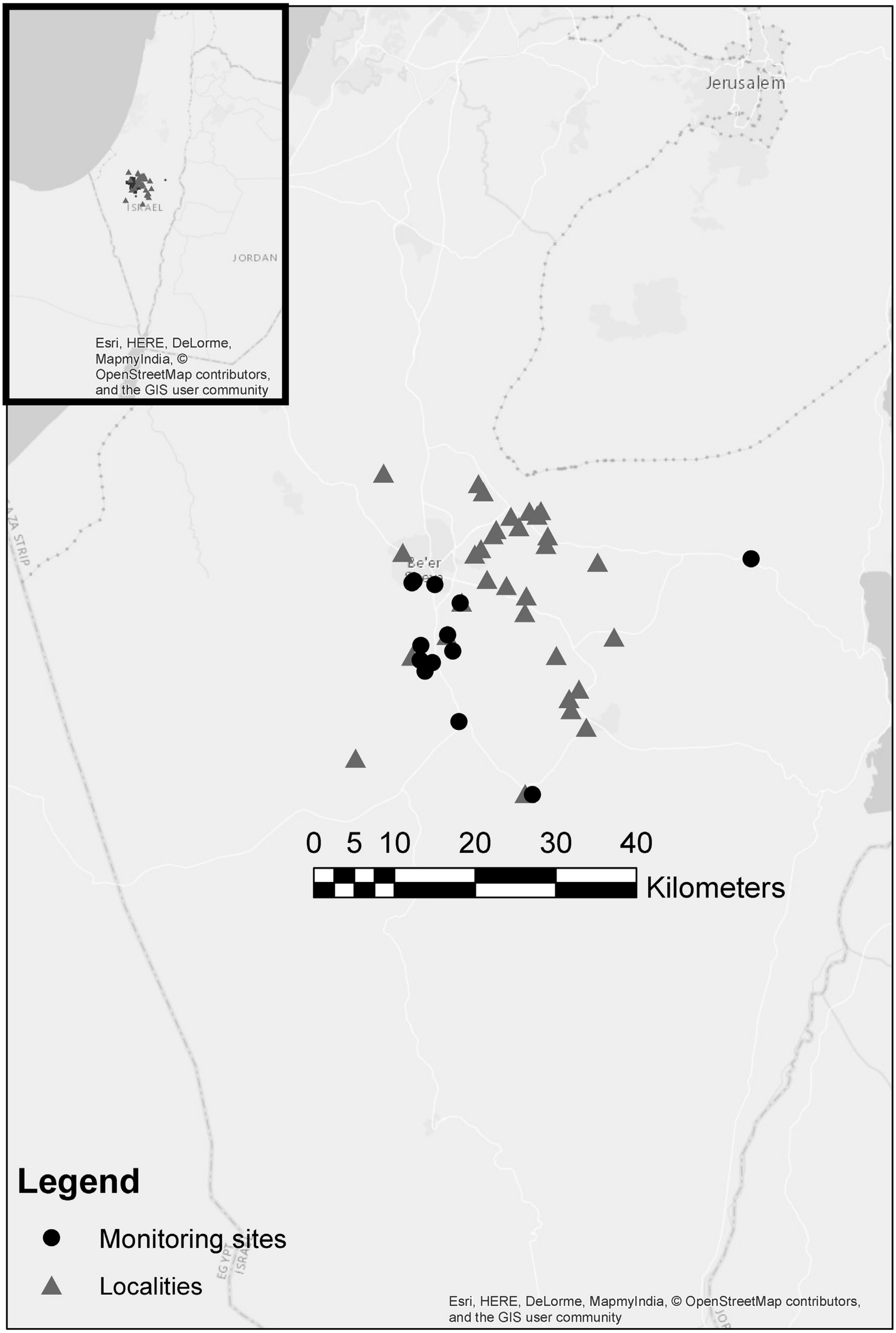

Fig. 1. Localities and monitoring sites in the study area.

Table 1
Maternal and birth characteristics.

Maternal and birth characteristics	Temporary locality 49% (473)	Permanent locality 51% (486)	P value
Maternal and Pregnancy Characteristics			
Maternal age, Years			
Mean ± SD	28.16 ± 6.00	28.14 ± 5.97	0.957
Parity			
Median (Min;Max)	4.00 (1; 13)	3.00 (1; 14)	0.188
Gestational age at birth, days			
Mean ± SD	276.92 ± 10.93	275.96 ± 9.45	0.046
Confirmed Diabetes Mellitus, %(n)	4.0% (19)	2.5% (12)	0.203
Abnormal glucose levels, %(n)	7.6% (36)	6.2% (30)	0.444
Hypertension, %(n)	0.6% (3)	0.8% (4)	1.000
Repeated abortions	5.7% (27)	5.6% (27)	1.000
Infertility treatment	0.8% (4)	1.6% (8)	0.385
Lack of prenatal care, % (n)	11.6% (55)	8.0% (39)	0.065
Birth Outcomes			
Weight at birth			
Mean ± SD	3247.14 ± 474	3278.08 ± 450	0.300
Male gender, % (n)	51.6% (244)	53.5% (260)	0.561

Table 2
Environmental exposures.

Environmental exposures and home environment (n = 959)	Temporary locality 49% (473)	Permanent locality 51% (486)	P value
Complaints on environmental disturbances:			
Dust, % (n)	88.7% (339)	88.7% (346)	1.000
Noise,% (n)	12.8% (49)	13.8% (54)	0.751
Waste, %(n)	12.8% (49)	12.1% (47)	0.745
Sewage, %(n)	32.7% (125)	24.4% (95)	0.010
Car usage, %(n)	49.0% (187)	41.5% (162)	0.043
Use of chemical fertilizer	12.6% (48)	4.1% (16)	<0.01
Use of pesticides, % (n)	78.5% (300)	73.1% (285)	0.078
Cooking with open fire, % (n)	33.8% (129)	6.4% (25)	<0.001
Form of heating, % (n)			
Electric	21.8% (76)	60.1% (220)	<0.001
Central	0.3% (1)	1.6% (6)	
Diesel/wood stove	49.4% (172)	33.6% (123)	
Open fire	28.2% (98)	4.6% (17)	
No heating	0.3% (1)	0.0% (0)	

Table 2 shows the complaints on environmental disturbances among women who reside in temporary localities compared to permanent localities. The presented results correspond to the percent and number of women who answered yes to each question.

the BW. The effects were slightly more pronounced in the third trimester, compared to only the last month of pregnancy; O_3 IQR (22.14 μg/m^3) elevation was associated with 0.234 gr decrease (95% CI −0.402 gr; −0.064 gr) in BW, and IQR elevation in temperature

Table 3
Air pollution, meteorological and other environmental exposures and the change in birth weight. Results of three Generalized Estimation Equation (GEE) models for repeated measures of Ozone and temperature during: (a) the entire pregnancy, (b) the third trimester and (c) the last month of pregnancy.

Variable	Change in birth weight (g) and 95% confidence intervals (CI)		
	(a) The entire pregnancy	(b) Last trimester[1]	(c) Last month[1]
Ambient exposures			
Ozone, 1 μg/m^3	−0.0005 (−0.0012; 0.0001)	−0.0106 (−0.0182; −0.0029)**	−0.0033 (−0.0058; −0.0009)**
Temperature, 1 °C	−0.0018 (−0.0031; −0.0005)**	−0.0219 (−0.0361; −0.0077) **	−0.0054 (−0.0090; −0.0018)**
Ozone* Temperature	0.0001 (0.0000; 0.0001)**	0.0009 (0.0004; 0.0015)**	0.0003 (0.0001; 0.0004)**
SO_2, 1 μg/m^3	0.0020 (0.0008; 0.0032)**	0.0165 (0.0063; 0.0268)**	0.0044 (0.0018; 0.0069)**
Household exposures			
Waste/Trash	−117.27 (−209.20; −25.34)**	−117.27 (−209.19; −25.34)**	−117.27 (−209.20; −25.34)**
Permanent locality	57.22 (−1.64; 116.09)*	57.21 (−1.64; 116.07)*	57.22 (−1.64; 116.09)*
Maternal and neonatal factors			
Gestational age at birth	17.53 (13.95; 21.11)**	17.53 (13.95; 21.11)**	17.53 (13.95; 21.11)**
Maternal age at birth	13.85 (8.30; 19.39) **	13.85 (8.30; 19.39)**	13.85 (8.30; 19.39)**
Maternal abnormal glucose levels	157.36 (37.15; 277.58)**	157.38 (37.17; 277.60)**	157.37 (37.15; 277.59)**
Male gender	133.05 (74.49; 191.61)**	133.05 (74.49; 191.61)**	133.05 (74.49; 191.62)**

Table 3 shows the change in birth weight associated with environmental exposures. Air pollution and meteorological data were retrieved from monitoring stations located within a 20 km radius of the participants' home address. Daily average pollutants' concentrations were interpolated to all localities in the study area using the a method of inverse distance weighting, in which every address was assigned a weighted average of the observed values in all available monitoring sites within 20 km radius. Results are presented per one unit increase of Ozone (1 μg/m^3), temperature (1 °C) and Sulfur Dioxide (1 μg/m^3).
**P < 0.05.
*p < 0.1.

(1.3 °C) was associated with 0.002 gr (95%CI −0.004 gr; −0.001 gr) decrease in BW (Table 3).

We found positive significant associations with SO_2 measured in the last month, the 3rd trimester and the entire pregnancy. We observed a significant decrease of 117.27 gr in BW associated with complaints on waste in the house surroundings (95% CI −209.19 gr; −25.34 gr); and a nearly significant increase of approximately 57 gr in BW associated with residence in a permanent locality (p = 0.05) (Table 3). Dust (−28.077 gr, 95%CI −128.618 gr; 72.463 gr), noise (6.111, 95%CI −87.645 gr; 99.867 gr), and sewage (25.560 gr, 95%CI −43.460 gr; 94.582 gr) complaints were not associated with birth weight. Birth weight was not associated with heating by open fire as well (−4.099 gr, 95%CI −87.613 gr; 79.591 gr). No other associations were found with any other pollutants (Supplementary Table 3).

Based on the stratified analysis by the type of locality, newborns of women residing in temporary housing were affected by different environmental factors compared to women living in permanent localities. In temporary localities, decrease in BW was more impacted by LOPC status (a nearly significant 110.69 gr decrease (95%CI −236.16 gr; 14.78 gr) and complaints on waste in the house surroundings (150.64 gr decrease (95% CI −294.73 gr; −6.54 gr). Newborns of women in permanent localities were more impacted by O_3 changes; IQR increase of O_3 concentrations during the 3rd trimester of pregnancy was significantly associated with 0.436 gr decrease (95% CI −0.790 gr; −0.081 gr) in BW. Similarly, the associations with temperature and SO_2 were stronger among women residing in permanent localities; an IQR increase of daily mean temperature was associated with 0.061 gr decrease in BW (95% CI −0.105 gr; −0.016 gr) and IQR increase of SO_2 (1.36 $\mu g/m^3$) was associated with 0.033 gr increase in BW (95% CI 0.008 gr; 0.004 gr) (Table 4).

In a stratified analysis by the season in the last trimester we observed stronger association with O_3 in pregnancies with the last trimester during the winter period (0.354 gr decrease in BW associated with IQR elevation in O_3, 95%CI: −0.717 gr; −0.003 gr) compared to in pregnancies with the last trimester during the summer period (0.013 gr decrease in BW associated with IQR elevation in O_3, 95%CI: −0.568 gr; 0.264 gr).

4. Discussion

We found significant reduction in BW associated with O_3 and temperature concentrations in the 3rd trimester and the last month of gestation. Although associations with ambient pollutants observed in the study were weak, their impact was slightly more pronounced among women residing in permanent localities. A stratified analysis by season revealed stronger association with O_3, if the last trimester was in winter. Among the individual factors, waste, an indicator of poor household environment, was more highly associated with BW, especially among women residing in temporary localities. The association observed with waste in the house surrounding might be directly associated with the exposure to hazardous components and indirectly with lower SES.

4.1. Biological mechanism

The vulnerability of pregnant women to temperature changes during gestation (Strand et al., 2011), can be explained by reduction of placental weight following maternal response to high temperatures, which may impair uterine and umbilical cord blood flow and reduce the availably of oxygen and glucose to the fetus (Wells, 2002). Regarding air pollution, biological mechanisms that may explain the impact of air pollution on adverse birth outcomes include suppression of the antioxidant defense system (Tabacova et al., 1998; Shah and Balkhair, 2011) and induction of inflammatory response in the fetus (Shah and Balkhair, 2011; Maroziene and Grazuleviciene, 2002). The mechanism in which O_3 may affect BW is unclear (Shah and Balkhair, 2011).

4.2. Temperature and air pollutants

Evidence of the association between temperature exposure during gestation period and BW are scarce and inconclusive (Lawlor et al., 2005; Deschenes et al., 2009; Flouris et al., 2009; Elter et al., 2004; Murray et al., 2000). Temperature related health effects may vary geographically, partially due to acclimatization to local weather conditions (Lee et al., 2014). A recent review found that the different seasonal patterns of BW, reported in different geographic locations, can be grouped according to latitude (Chodick et al.,

Table 4
Stratified analysis by the type of locality. Generalized Estimation Equation (GEE) results for repeated measures of Ozone, SO_2 and temperature during the third trimester of pregnancy among women residing in permanent (a) and temporary (b) localities.

Variable	Change in birth weight (g) and 95% confidence intervals (CI)	
	(a) Permanent locality	(b) Temporary locality
Ambient exposures		
Ozone, 1 $\mu g/m^3$	−0.0197 (−0.0357; −0.0037)**	−0.0014 (−0.0022; −0.0005)**
Temperature, 1 °C	−0.0470 (−0.0814; −0.0127)**	−0.0015 (−0.0033; 0.0003)
Ozone* Temperature	0.0018 (0.0006; 0.0030)**	0.0001 (0.0000; 0.0002)**
SO_2, 1 $\mu g/m^3$	0.0246 (0.0006; 0.0030)**	0.0015 (0.0001; 0.0029)**
Household exposures		
Waste/Trash	–	−150.64 (−294.73; −6.54)**
Maternal and neonatal factors		
Gestational age at birth	20.73 (16.96; 24.50)**	13.49 (8.78; 18.19)**
Maternal age at birth	13.47 (7.31; 19.64) **	14.78 (6.78; 22.78)**
Maternal abnormal glucose levels	179.44 (31.10; 327.78)**	–
Male gender	127.71 (57.56; 197.85)**	172.47 (87.04; 257.91)**
LOPC	–	−110.69 (−236.16; 14.78)*

Table 4 show the change in birth weight associated with environmental exposures, stratified by the type of locality. The models include factors which were found significant at the level of p-value < 0.1, at least. Results are presented per one unit increase of Ozone (1 $\mu g/m^3$), temperature (1 °C) and Sulfur Dioxide (1 $\mu g/m^3$).
**P < 0.05.
*p < 0.1.

2009). A study performed in Israel found maximal BW during summer seasons and minimal BW during winter seasons (Chodick et al., 2007). Other studies exploring seasonal variations in low-latitude regions reported similar results (Matsuda et al., 1995; McGrath et al., 2005). In contrast, in areas of high latitude (such as Scotland and Denmark) low BW was more common in the winter season (Lawlor et al., 2005; McGrath et al., 2007). Given the different findings, partially due to different definition of seasons and local geographical characteristics, a consistent conclusion cannot be established yet (Beltran et al., 2014). To illustrate this point, the current study was performed in a low latitude area with prevailing hot and dry climate. The air pollutants measured in the study varied substantially between hot and cold seasons, with PMs being lowest in colder and rainy seasons, and CO and SO_2 reaching their extreme values in winter and spring and O_3 – in spring and summer (Supplementary Tables 1 and 2). The effect of pollutants and temperature should therefore be investigated together, and being specific to certain types of climate.

4.3. Sulfur dioxide

Unlike studies that reported decreased BW following exposure to SO2 (Lin et al., 2004; Bobak, 2000; Maisonet et al., 2001), we found positive associations between maternal exposure to SO2 during pregnancy and BW. A study performed in a neighboring country found that SO2 concentrations were strongly related to cold temperatures, lower precipitation and higher relative humidity (Turalioglu et al., 2005). Another study found significant interaction between temperatures, ozone and SO2 (Katsouyanni et al., 2009). The South Israeli region is a desert area characterized with high temperatures and negligible precipitation most of the year, it therefore possible that the association found with SO2 is due to residual confounding by meteorological parameters.

In accordance with our findings, Gouveia and colleagues found positive associations between BW and maternal exposure to SO2 in the second trimester of pregnancy (Gouveia et al., 2004). Similarly, a meta-analysis reported a pooled estimate of 7.3 g increase in BW associated with 5 ppb increase of SO2 exposure during the entire gestation period (Stieb et al., 2012). Possible explanations of the positive associations found with SO2 may be due to unmeasured confounders, (Ha et al., 2014) or exposure misclassification error.

4.4. Ozone

Current studies contradict in reporting of the association between O3 exposure in pregnancy and BW. A recent review reported that most studies found no significant associations with O3 (Ha et al., 2001; Chen et al., 2002; Gouveia et al., 2004; Dugandzic et al., 2006; Lin et al., 2004; Shah and Balkhair, 2011; Liu et al., 2003), the majority of these studies (Ha et al., 2001; Gouveia et al., 2004; Dugandzic et al., 2006; Liu et al., 2003) were not adjusted for temperature. O3 is a secondary pollutant produced by photochemical reactions and for that reason is highly influenced by sun intensity and temperature. Thus, higher O3 concentrations are observed in warmer seasons (Lavee et al., 2015).

On the other hand, significant reduction in BW was associated with O3 in two analyses where the effect was adjusted for monthly temporal variations or season of birth (Morello-Frosch et al., 2010; Salam et al., 2005). In the first study, which included over three million singleton births, 5.7 gr decrease in BW was associated with exposure to increase of 1 pphm O3 average concentrations in the entire gestation period (Morello-Frosch et al., 2010). In the second, researchers in the children's health study in California showed a significant reduction of 35.2 gr in BW, associated with 17 ppb increase of O3 average concentrations in the third trimesters of pregnancy (Salam et al., 2005). The different level of adjustment, especially to temperature, may explain the difference in the studies' conclusions.

4.5. BW

SES characteristics may confound the association between environmental exposures and birth outcomes (Gray et al., 2014; Zeka et al., 2008). The question remains whether mothers with low SES are more likely to reside in high polluted areas or whether exposure to air pollution is independently associated with adverse birth outcomes (Woodruff et al., 2003). According to the Central Bureau of Statistics, all Bedouin settlements are ranked in the lowest cluster of SES [62]. Given that, we were not able to properly examine interactions with SES. We found a weaker association with Ozone and temperature among women residing in temporary settlements compared to permanent cities. However, other than serving as an indicator for low SES levels, the type of residence can also represent poor household environment.

4.6. Strengths and limitations

The major strength of our study is the inclusion of a wide range of environmental exposures for the investigation of the link between these environmental factors and birth weight in a large study population. Among women who reside in temporary locality in particular, the outdoor pollutants' measurements are expected to approximate the indoor measurements due to higher pollution infiltration. Additionally, the population included in our study is featured by low socio-economic levels and poor housing and household environment, and therefore serve as an important target population for the investigation of environmental exposures and birth outcomes.

Our study had several limitations. First, air pollution and meteorology data were not available in all monitoring sites; in addition we assigned exposure based on ambient air pollution concentrations, which may have resulted in exposure misclassification. However, in attempt to reduce exposure misclassification, daily average pollutants concentrations were interpolated to all localities in the study area using the method of inverse distance weighting. Second, exposure was obtained from monitoring sites and was linked to each woman based on the distance from the center of the locality of residence, and not at a resolution of an exact address. It may have resulted in exposure misclassification bias yielding the effect towards the '0' hypothesis. Lastly, we were not able to adjust our models for maternal smoking, as 100% of the women stated that they did not smoke, possibly due to an information bias in the data collection stage. .

5. Conclusion

Exposure to increased levels of temperature and O_3 were associated with lower BW. The contribution of poor household environment indicators to BW reduction was substantially higher.

Conflict of interest

None of the authors have any competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.chemosphere.2016.06.104.

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