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Is air quality index associated with cardiometabolic risk factors in adolescents? The CASPIAN-III Study

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ABSTRACT

Objective: This study aims to evaluate the association of air quality index (AQI) with cardiometabolic risk factors in a nationally representative sample of healthy adolescents.
Methods: This nationwide survey was conducted among a stratified multi-stage probability sample of students, aged 10–18 years, from 27 provinces of Iran. Those students with history of any acute or chronic diseases, any medication use, as well as active or passive smoking were not included to the current study. Dietary and physical activity habits were documented by valid questionnaires. Physical examination and blood sampling were conducted under standard protocols. AQI data were obtained from air pollution monitoring sites from the entire country by considering air pollutants concentration, which includes all provincial counties containing different clusters.
Results: The study participants consisted of 1413 students (48.8% boys) with a mean (SD) age of 14.81 ± 2.48 years. The mean AQI level was 285.37 ± 30.11 at national levels. After adjustment for confounding factors including age, sex, and anthropometric measures, as well as for dietary and physical activity habits, multiple linear regressions based on correlation of coefficients of the AQI with cardiometabolic risk factors showed significant positive correlations of AQI with systolic blood pressure, fasting blood glucose, total cholesterol, LDL-cholesterol, and triglycerides, as well as significant negative correlations with HDL-cholesterol. After adjustment for abovementioned confounding factors, binary logistic regressions analyses showed that AQI increased the risk of abnormal levels of some risk factors as elevated levels of systolic blood pressure, total cholesterol, and triglycerides.
Conclusion: The associations of low air quality with some cardiometabolic factors in the current survey, although not strong, might be considered as an evidence of the adverse cardiometabolic consequences of exposure to air pollutants in the pediatric age group, and predisposing them to earlier development of non-communicable diseases.

1. Introduction

Non-communicable diseases (NCDs) are the commonest cause of the burden of diseases and the leading cause of death worldwide, with an escalating trend notably in the low-and middle-income countries (Di Cesare et al., 2013). Early identification of their predisposing factors is necessary for primary prevention and early management of chronic diseases.

Although in recent decades, a growing body of evidence proposed that early life risk factors may affect the development of NCDs and their risk factors in adulthood (Sun et al., 2014; Kent, 2012), the current research is mostly focusing on adulthood rather than poorly understood period of childhood and adolescence in the development of adulthood diseases.

It is well documented that ambient air pollution increases the risk of the major NCDs including diabetes mellitus (Rajagopalan and Brook, 2012), cardiovascular diseases (Hoek et al., 2013), and cancers (de Groot and Munden, 2012). Similarly, exposure to air pollutants in childhood may have long-term adverse effects on the beginning and progression of such chronic diseases, and thereby predisposing them to earlier development of risk factors and disease later in life.

The air quality index (AQI) is developed by the U.S. Environmental Protection Agency (www.epa.gov/aqi), and can be used to

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describe the harmfulness of air pollution levels. It includes five major air pollutants: ground-level ozone, particulate matter, carbon monoxide, sulfur dioxide, and nitrogen dioxide. AQI values above 100 are considered to be unhealthy for sensitive groups, then for everybody as AQI values get higher.

Limited number of population-based studies has evaluated the association of air quality with risk factors of NCDs in healthy children and adolescents. These studies have shown that recent exposure to air pollutants is associated with increases in blood pressure (BP), heart rate, arterial stiffness, systemic inflammation, oxidative stress, insulin resistance, and endothelial dysfunction (Iannuzzi et al., 2010; Calderon-Garciduenas et al., 2008; Kelishadi et al., 2009, 2007).

Most of these studies have been conducted on small number of children and adolescents living in a single region. To the best of our knowledge, none of the previous studies has evaluated a large sample of pediatric population with nationwide distribution for such health effects.

The current study aims to evaluate the association of AQI with cardiometabolic risk factors in a nationally representative sample of healthy adolescents.

2. Methods

The data of this multi-centric cross-sectional study were collected as a part of the "national survey of school student high risk behaviors" (2009–2010) as the third survey of the school-based surveillance system entitled Childhood and Adolescence Surveillance and Prevention of Adult Non-communicable disease (CASPIAN-III) Study. This nationwide school-based health survey was conducted in 27 provinces in Iran. Details on the study protocol have been described before (Kelishadi et al., 2012), and here we report it in brief.

Study protocols were reviewed and approved by ethics committees and other relevant national regulatory organizations. We obtained signatures of parents on written informed consent form and verbal assent from students.

A stratified multi-stage probability sample of students aged 10–18 years was selected from urban and rural districts of 27 provinces of Iran. Those students with history of any acute or chronic diseases, any medication use, as well as history of active or passive smoking were not included in the current study.

Two sets of questionnaires were prepared for students and parents. The questionnaires of students were based on the World Health Organization-Global School Health Survey (WHO-GSHS). The validity of their content was affirmed based on observations of an experts' panel and item analysis. Reliability measures were assessed based on a pilot study. The questionnaires were filled out confidentially under the supervision of trained nurses (Kelishadi et al., 2012).

As described before, for assessing dietary habits, we used questions about the type of bread (i.e. prepared from white or wholegrain flour) and the type of fat consumed in meals at home. In addition, students completed a validated food-frequency questionnaire (FFQ). Food items were grouped into the following categories: carbohydrates (rice, bread, pasta, potato), vegetables (potato and French fries not included), fruit (fresh, dried, juice), dairy products (milk, cheese, yogurt), proteins, including both animal-derived (red meat, poultry, fish, egg) and plant-derived (beans, soy, nuts), fast foods (pizza, hamburgers, sausages etc.), as well as salty/high fat snacks and sweets/candies. We calculated unhealthy foods consumption as a continuous variable by factor analysis (principle component). To evaluate the pattern of physical activity, three indicators were used including: (i) hours of physical education at school; (ii) hours of watching television at home; and (iii) hours spent on sport club training (Kelishadi et al., 2013).

A team of expert physicians, nurses, and healthcare providers conducted the physical examination according to standard protocols, and by using calibrated instruments. Weight and height were measured; body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist circumference was measured using a non-elastic tape at a point midway between the lower border of the rib cage and the iliac crest at the end of normal expiration to the nearest 0.1 cm. Overweight and obesity were defined according to the WHO growth curves i.e., overweight as sex-specific BMI for age of $> +1$ z-score, and obesity as sex-specific BMI of $> +2$ z-score (de Onis et al., 2007). Systolic and diastolic BP (SBP and DBP) were measured under standard protocol by using calibrated mercury sphygmomanometers and appropriate size cuff (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004). Fasting venous blood sample was examined for fasting blood glucose (FBG) and lipid profile. In each district, the biochemical analysis was performed in the Central Provincial laboratory, which met the standards of the National Reference laboratory, a WHO collaborating center in Tehran. The fresh sera were tested by Pars Azmoon reagents kit (Tehran, Iran). Abnormal levels of risk factors were considered as follows: total cholesterol (TC) >200 mg/dL, low density lipoprotein–cholesterol (LDL–C) >110 mg/dL, triglycerides (TG) ≥ 100 mg/mL, high density lipoprotein–cholesterol (HDL–C) <50 mg/dL (in 15 to18-year-old boys <45 mg/dL), FBG ≥ 100 mg/dL (Balagopal et al., 2011), and BP $\geq$ 95th percentile (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004).

Data on the air quality index (AQI) were obtained from the Iranian Department of Environment, which is a governmental organization, and collects data from all air pollution-monitoring sites of the country using the same standards and equipment (www.doe.ir). The mean AQI values from the study time till one year prior to the survey were used in this study. These data were obtained from the North, South, Central, East, and West parts of the country by considering the concentration of air pollutants of all provincial counties containing different clusters.

2.1. Statistical analysis

Data were entered into the data-collection sheet, then they were digitally entered and analyzed. Mean and standard deviation (SD) were used to describe the cardiometabolic risk factors of the sample-based on different geographic regions. Multiple linear regression analyses, considering two different adjusted strategies were conducted to examine the relationship between the AQI and cardiometabolic risk factors through Stepwise and Enter methods. In the regression modeling, each cardio-metabolic risk factor (SBP, DBP, FBG, TC, LDL–C, HDL–C, and TG) was considered as dependent variable and AQI as independent variable. In the first model, we adjusted the analysis for age and sex; in the second model, in addition to sex and age, the analysis was adjusted for BMI, waist circumference, diet and physical activity.

In addition, regression (R) and determination coefficients (R^2; >0.7) were verified and estimate standard, as well as total errors were calculated. Multi-collinearity was examined by variance inflation factor (not shown).

Binary logistic regressions were conducted based on correlation of coefficients of the AQI with abnormal levels of cardiometabolic risk factors. Two models were considered: in Model1, the analyses were adjusted for age and sex; in Model2, adjustment was done for age, sex, BMI, waist circumference, dietary and physical activity habits.

$P<0.05$ was considered as statistically significant. Statistical analyses were performed with SPSS version 20.0 (IBM, Armonk, NY, USA).

3. Results

Data of AQI were complete for 1413 students (48.8% boys), and are included in the analyses. The mean (SD) age of participants was 14.81 ± 2.48 years without significant difference in terms of sex. The mean AQI level was 285.37 ± 30.11 at national levels, with highest and lowest levels in the North and the East regions, respectively. In general, the mean AQI value indicated poor air quality, which corresponded to unhealthy levels for the study population.

Table 1 presents the mean (SD) levels of AQI and cardiometabolic risk factors at national and regional levels. It shows significant differences between different regions based on the AQI mean measure. After adjustment for confounding factors including age, sex, BMI, and waist circumference, as well as for dietary and physical activity habits, multiple linear regressions based on correlation of coefficients of the AQI with cardiometabolic risk factors showed significant positive correlations of AQI with SBP, FBG, TC, LDL–C, and TG, as well as significant negative correlations with HDL–C (Table 2).

Results of binary logistic regressions of AQI with abnormal levels of cardiometabolic risk factors are presented in Table 3. After adjustment for age and sex, in some regions AQI significantly increased the risk of elevated SBP and FBG, as well as lipid disorder in terms of elevated TC and HDL–C and low HDL–C. After further adjustment for BMI, WC, diet and physical activity, it remained significant for elevated FBG, TC, and TG.

4. Discussion

In the current study, we found some associations between low air quality and some cardiometabolic risk factors among a sample

Table 1
Mean (SD) of the air quality index and cardiometabolic risk factors in Iranian adolescents at national and regional level: the CASPIN-III Study.

Geographical region	AQI	*N*	SBP	DBP	FBG	TC	LDL–C	HDL–C	TG
National	285.37 (30.11)	1413	103.19 (13.9)	69.95 (11.13)	87.53 (11.94)	147.83 (30.59)	89.11 (2.54)	43.09 (10.96)	91.81 (4.63)
North	540.16 (53.82)	463	104.26 (14.67)	64.46 (11.19)	87.27 (12.31)	145.59 (32.40)	88.07 (3.07)	41.87 (10.01)	93.27 (4.09)
South	94.44 (27.69)	202	102.08 (12.73)	64.94 (10.65)	87.67 (12.57)	139.21 (31.79)	80.37 (2.09)	46.42 (11.02)	89.45 (3.89)
Center	371.13 (57.8)	277	102.79 (12.10)	65.12 (11.04)	88.91 (10.16)	155.45 (30.60)	92.37 (2.53)	42.99 (11.01)	91.38 (4.80)
West	200.03 (63.12)	233	100.61 (14.63)	63.12 (10.64)	88.29 (11.58)	153.64 (25.91)	91.49 (2.09)	44.23 (8.65)	99.23 (4.32)
East	74.99 (91.18)	238	103.02 (14.25)	64.56 (11.69)	87.98 (12.36)	150.55 (29.35)	92.39 (2.88)	41.93 (10.03)	80.8 (2.65)

SD: standard deviation; AQI: air quality index; SBP: systolic blood pressure (mmHg); DBP: diastolic blood pressure (mmHg); FBG: fasting blood glucose (mg/dL); TC: total cholesterol (mg/dL); LDL–C: low density lipoprotein–cholesterol (mg/dL); HDL–C: high density lipoprotein–cholesterol (mg/dL); TG: triglycerides (mg/dL).

Table 2
Results of multiple linear regressions based on correlation of coefficients of the air quality index with cardiometabolic risk factors in Iranian adolescents at national and regional levels: the CASPIN-III Study.

Geographical region	SBP		FBG		TC		LDL–C		HDL–C		TG	
	Model1	Model2	Model1	Model2	Model1	Model2	Model1	Model2	Model1	Model2	Model1	Model2
National	0.782*	0.012	0.001	0.012	0.010	0.003	0.204*	0.016	−0.007	−0.016	0.007	0.006
North	0.001	0.068	0.007	0.014	0.021	0.006	0.405*	0.026	−0.014	−0.027	0.011	0.261*
South	0.010	0.035	0.014	0.020	0.009	0.004	0.010	0.018	−0.017	−0.039	0.019	0.028
Center	0.205*	0.097	0.232*	0.319*	0.255*	0.201*	0.321*	0.021	−0.300*	−0.443*	0.085	0.017
West	0.105*	0.107*	0.114*	0.158*	0.137*	0.001	0.120*	0.088	−0.117*	−0.136*	0.092	0.021
East	0.801*	0.011	0.137*	0.071	0.109*	0.107	0.098	0.050	−0.182*	−0.183*	0.149*	0.216*

Model1: adjusted model by age and sex; Model2: adjusted model by age, sex, body mass index, waist circumference, diet and physical activity.
None of the results of the analyses for diastolic blood pressure was significant, and therefore not included in the table.
SBP: systolic blood pressure (mmHg); FBG: fasting blood glucose (mg/dL); TC: total cholesterol (mg/dL); LDL–C: low density lipoprotein–cholesterol (mg/dL); HDL–C: high density lipoprotein–cholesterol (mg/dL); TG: triglycerides (mg/dL).

* *P*-value < 0.05.

Table 3
Odds ratio for the association of the air quality index with abnormal levels of cardiometabolic risk factors in Iranian adolescents at national and regional levels: the CASPIN-III Study.

Geographical region	Elevated SBP		Elevated FBG		Elevated TC		Elevated LDL–C		Low HDL–C		Elevated TG	
	Model1	Model2	Model1	Model2	Model1	Model2	Model1	Model2	Model1	Model2	Model1	Model2
National	1.926*	1.002	1.001	1.001	1.001	1.002	2.010*	1.010	0.987	0.998	1.000	1.001
North	1.120	1.117	1.080	1.008	1.023	0.897	0.786*	1.009	0.876	0.986	1.003	2.821*
South	1.150	1.120	1.040	1.002	1.001	0.913	1.002	0.997	0.776	0.974	1.098	1.030
Center	1.260	1.130	1.987*	1.875*	1.779*	0.989*	1.001*	1.005	0.432*	0.913	0.981	0.978
West	1.579*	1.067	1.087	1.043	1.033	1.001	1.876*	1.003	0.543*	0.456	1.002	1.000
East	2.013*	1.030	1.675*	0.987	0.976	1.003	1.000	0.999	0.954	0.876	2.109*	2.012*

Model1: adjusted model by age and sex; Model2: adjusted model by age, sex, body mass index, waist circumference, diet and physical activity.
None of the results of the analyses for diastolic blood pressure was significant, and therefore not included in the table.
SBP: systolic blood pressure (mmHg); FBG: fasting blood glucose (mg/dL); TC: total cholesterol (mg/dL); LDL–C: low density lipoprotein–cholesterol (mg/dL); HDL–C: high density lipoprotein–cholesterol (mg/dL); TG: triglycerides (mg/dL). The abnormal levels were defined as: low HDL: < 50 mg/dL (except in boys 15–19 years old, that cut-off was < 45 mg/dL); high LDL–C: > 110 mg/dL; high TG: ≥ 100 mg/dL; high TC: > 200 mg/dL; high FBG levels of ≥ 100 mg/dL [(Balagopal et al., 2011)]; elevated BP $\geq$ 95th percentile [(National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004)].

* *P*-value < 0.05.

of healthy adolescents. Although these associations were not strong, they might serve as confirmatory evidence on the cardiometabolic consequences of chronic exposure to ambient air pollutants from early life.

Environmental influences should be considered among predisposing factors for NCDs. Most evidence on the associations of ambient air pollutants with NCD risk factors comes from experimental studies and epidemiological surveys conducted among adults, very limited experience exists in the pediatric population.

Various mechanisms have been explained for the adverse cardiometabolic consequences of air-pollutants (Rajagopalan and Brook, 2012; Brook and Rajagopalan, 2010; Sun et al., 2013; Parnia et al., 2014). Some of these changes are even documented in the pediatric age group (Iannuzzi et al., 2010; Kelishadi et al., 2009, 2014, 2011; Hashemi et al., 2012). Experimental studies have also shown that exposure to fine particulate matter exaggerates insulin resistance and visceral inflammation/adiposity (X. Xu et al., 2011; Sun et al., 2005). In turn, inflammation in visceral adipose tissue and liver would dysregulate the glucose and lipoprotein metabolism. Moreover, the visceral adipose inflammation and oxidative stress are associated with changes in circulating levels of adipokines, as adiponectin and leptin (X. Xu et al., 2011; Z. Xu et al., 2011; Brook et al., 2008; Pearson et al., 2010). The effects of particulate air pollution on the development of metabolic disorders may be mediated by triggered cell stress response in adipose tissue (Mendez et al., 2013).

Epidemiologic and observational studies have consistently shown that depressed plasma levels of HDL–C represent an independent inverse predictor of atherosclerotic cardiovascular disease risk. Several studies in the Middle East, including national

studies in Iran, revealed a markedly high prevalence of this disturbance in adults (Delavari et al., 2009), as well as in children (Kelishadi et al., 2007). The reasons of the very high prevalence of this lipid disorder remain speculative, and in addition to genetic and lifestyle habits, environmental factors may have a role in this regard. The current study suggests that the high prevalence of depressed HDL–C in Iranian children and adolescents, even in those without excess weight (Kelishadi et al., 2008), can be in part because of their chronic exposure to ambient air pollutants. The underlying mechanisms of the effects of exposure to air pollutants on HDL–C remain to be determined. According to a recent experimental study, paraoxonase enzymatic activity may have a role in this regard (Yin et al., 2013).

Ample evidence exists about the effect of air pollutants on elevated BP and the development of prehypertension and hypertension. This effect is found to be independent of major cardiovascular risk factors as age, diabetes, dyslipidemia and obesity. It is well documented that exposure to ambient air pollution may increase BP within hours to days (Roman et al., 2009; Walker and Mouton, 2008; Brook, 2007; Poursafa and Kelishadi, 2011). This association may be mediated through autonomic nervous system imbalance and arterial vascular dysfunction or vasoconstriction. The traffic-related exposure to air pollutants may increase systolic BP, and in turn left ventricular mass index (O'Neill et al., 2011). Our findings are in line with a study in Pakistan that showed associations for air pollutants and increase in SBP and DBP in 8 to12-year-old children (Sughis et al., 2012). Air pollution is a worldwide challenge for the public and individual health. Epidemiological and experimental studies have revealed consistent results on the adverse cardiometabolic consequences of ambient air pollutants, and in turn on the development of NCDs, mainly cardiovascular diseases and diabetes (Rajagopalan and Brook, 2012; Hoek et al., 2013). A main challenge to understand the adverse effects of exposure to ambient air pollutants is the complex nature of genetic, environmental and behavioral influences. Metabolic profile is highly affected by genetic, sex, diet, physical activity, tobacco use, weight status, medical history, and the process of aging. In the current study, we reduced the role of these factors by studying a very young population without underlying health disorder, and by adjusting for other confounders.

Our study has limitations including its cross-sectional nature. Future longitudinal studies are necessary to verify the associations documented in the current study and to document their clinical significance. Moreover, personal exposure to air pollutants was not recorded. The biological and biochemical measurements were taken on just one day, which did not account for inter-day variability. In our study, large variations existed in the AQI of different parts of the country; this is because in some parts of the country as the Southern region, dust is a major problem, whereas in the Central areas, the main sources of pollutants are industries and motor vehicles. Moreover, Iran has diverse climatic conditions, e.g. some parts are humid, some are mountainous, and some are desert and half-desert. We suggest that future studies should consider detailed information on the climatic and geographical conditions, as well as the source of pollutants in various regions. The other limitation is that we did not adjust the analyses for the meteorological variables that affect air pollutants, for instance weather may have different effects on air pollutants, e.g. higher air temperatures accelerate chemical reactions in the air, rain may wash out soluble pollutants, sunshine may increase smog production, and wind speed changes the dispersal of pollutants. Moreover, complex interactions are documented between ambient temperature and cardiometabolic risk factors, for instance higher air temperature might have beneficial effects in decreasing BP levels (Halonen et al., 2011; Hoffmann et al., 2012), but on the other hand it is associated with increase in harmful type of cholesterol (LDL–C) and decrease in its useful type (HDL–C) (Halonen et al., 2011). The main strengths of this study are its novelty in the pediatric age group, including a large nationwide sample size with widespread distribution, and adjusting the associations for most confounding factors.

5. Conclusion

We found that after adjustment for confounding factors including age, sex, BMI, and waist circumference, as well as for dietary and physical activity habits, AQI had significant positive correlations with SBP, FBG, TC, LDL–C, and TG, as well as significant negative correlations with HDL–C. The associations of low air quality with some cardiometabolic factors, although not so strong, can be considered as an evidence of the adverse cardiometabolic consequences of exposure to air pollutants in the pediatric age group. It can be proposed that chronic exposure to high levels of ambient air pollutants may be one of the mechanisms by which air pollution enhances the risk of chronic diseases, and over time it might predispose the children to earlier development of NCDs. Improving the air quality and limiting the exposure of children and adolescents to air pollutants should be considered among primordial/primary preventive measures for chronic diseases of adulthood.

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Data of this study were collected from a survey conducted as part of a national school-based surveillance system.

Conflict of interest

None to declare.

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