ORIGINAL ARTICLE

Assessment of Circadian Rhythmicity of Respiratory Determinants Related to Diurnal Activities of Children and Adolescents: A Case Study in the City of Isfahan

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Abstract

Background: Diurnal sequences of activities conducted at several locations visited by individuals have an impact on population exposure to air pollution. However, data on individual's movement with a fine time resolution is rare.
Methods: In the current study, 399 children and adolescents (aged 11–18 years) from Isfahan city were asked to recall their 24-hour diary during winter and spring 2014-2015. Daily ventilation rates for individuals were calculated using Consolidated Human Activity Database (CHAD) and were subject to cosinor analysis.
Results: There was a significant circadian rhythm in inhalation rate, outdoor time-spent and ambient NO_2 pollution. The ANOVA of rhythm parameters showed a significant difference ($P < 0.05$) between gender groups and day types, whereas the difference between age groups and seasons was not significant. Analysis of results showed that increased NO_2 pollution was concurrent with increased inhalation rate and outdoor time-spent. Inhalation rates obtained for population groups were 9.3, 11.6, 9.0 and 11.3 L/min for high school girls, high school boys, elementary girls and elementary boys, respectively. Elementary boys were at higher risk of exposure to air pollution. Boys spent more time outdoors and in traffic than girls. Respondents spent 89% of their time inside and 82% of their inside time at home. They also spent 10% of their time during a year in school. Respondents were exposed to cooking generated pollutants 11 times a week. Among them, 30% were exposed to second-hand smoke, and 86.3% reported in very good health.
Conclusion: We concluded that actual exposure levels may be underestimated when the simple risk assessment method is implemented without the survey of fine time resolution spatiotemporal activity data.

Keywords: Air Pollution; Exposure; Circadian Rhythm; Inhalation Rate; Risk

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INTRODUCTION

Unlike the past that clean air was available to all, contemporary children are exposed to a variety of air toxins from the moment of birth. Children and adolescents are considered one of the most susceptible population groups to air pollution due to their transition from several developmental and puberty stages. Children have higher inhalation rates, less rhinal contribution to breathing (1) and less efficiency of particle uptake in upper airways (2). Persistent organic pollutants are known to interfere with puberty in adolescents (3). Puberty coincides with behavioral changes, that can alter the exposure level to air pollution. Exposure of contemporary youngsters to air pollution would result in health problems that could adversely impact the quality of their future life as adults.

In response to health problems of environmental pollutants, exposure and risk assessment models were developed (4). Although such models demand precise data sets, due to the difficulty of gathering this data, scientists often assume the pollutant concentration within the breathing zone of a person is equal to average outdoor concentration, even a single inhalation rate is used for all hours and individuals. These simplifications may be misleading because more than 70% of the individual's time is spent indoors (5). In addition, new investigations have revealed the importance of differentiating microenvironments and the amount of time a person spends there (6). Consequently, for precise determination of population exposure to air pollution and finding opportunities for risk reduction, knowledge of daily activity pattern is necessary.

As there is a large difference in lifestyle among communities in regard to culture, religion and environmental living conditions, it is necessary to examine population activity in different communities around the world. In 1980, EPA provided the Consolidated Human Activity Database compiled from several studies conducted in the United States for use in Air Pollution Exposure Model (APEX) (4, 7, 8).

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Similar studies have been conducted in seven Canadian cities (9), Helsinki, Finland (10), and in Greater Manchester, England (11). To our best knowledge, activity-location diaries had not been surveyed in Asian moslem communities living mostly in arid regions.

Due to lack of precise information on spatiotemporal activity pattern in arid regions and about eastern lifestyle, the current study attemped to survey daily activities of the Isfahanian susceptible population subgroups (i.e., children and adolescents) spatially and temporally. The circadian rhythm of inhalation rate in relation to NO_2 pollutant's circadian variations was also investigated. The aim of the current study was to stablish social groups that are at the highest risk associated with exposure to air pollution in order to evaluate the extent of unequality in exposure levels among age and gender groups and determine which hours of a day are associated with highest exposure levels.

METHODS

Study population

In order to investigate the diary events of children and adolescents, i.e., the highest exposed population groups to air pollution, during winter 2014 and spring 2015, data were gathered from 200 boys and 225 girls (0.2% of total population of students) from eight elementary schools and high schools in two central educational regions of Isfahan. In Isfahan, the total number of children and adolescents aged 10-18 was 23988 of which 86% attended school (12). The selected educational regions (4 and 5) encompassed more than 50% of the population of Isfahanian students, located in mostly polluted central areas of the city (12). Two male and female retired teachers were invited to visit the boys' schools and girls' schools, respectively. Sampling was focused on two months, including January and May. Students went to school on average for 175-187 days, almost equal to half of the year. Therefore, sampling frequency was equal between holidays and schooldays. The average temperature was 6.6 °C in January and 23.7 °C in May. This study was approved by Preservation and Research Committee of Isfahan Education and Training Organization as well as a Research Council of Tarbiat-Modares University. All respondants provided written consent from their parrents.

Design of the questionnaire

Questionnaires were designed in two forms of self-report for school days and hourly-tabulated for holidays. Children filled a 24-hour diary asking for the activity, start/end times, and location for all the activities, including night sleep. For school days, the best precision level was 5 minutes, whereas for holidays the smallest duration of activity was one hour. Complementary questions included wake-up hour, time of exit for going to school mode of transport, health status, smoking family members, and weekly cooking frequency at home. Incomplete and unreadable diaries were removed. Finally, 399 diaries were coded according to the USEPA CHAD coding scheme (4), and they were analyzed for continuity and code correctness with a MATLAB script designed by authors.

Energy expenditure calculation

Metabolic equivalents of work (*METS*) for activities were obtained from U.S. EPA's Consolidated Human Activity Database (CHAD) (13). Energy expenditure (*EE*, kcal/min) was calculated as:

$$EE = BMR \times METS \times 0.16587$$

where *BMR* is the basal metabolic rate (MJ/day) that is calculated for males and females separately by (13):

Male: $BMR = 0.074 \times BW + 2.754$

Female: $BMR = 0.056 \times BW + 2.898$

Inhalation rate calculation

The inhalation rate calculation method is obtained from EPA (13). In summary, VO_2 was calculated as the product of *EE* (kcal/min) and *H*, the volume of oxygen consumed per unit of energy (L O_2/kcal):

$$VO_2 = EE \times H.$$

H was 0.21 for boys and 0.20 for girls.

The following multiple linear regression model was used for predicting body-weight adjusted ventilation rate (V_E/BW; L/min/kg) as a function of VO_2 (after adjusting for individual's body weight), gender, and age:

$$\ln (V_E/BW) = 4.4329 + 1.0864 \times \ln (VO_2/BW) - 0.2829 \times \ln (age) + 0.0513 \times gender$$

BW denotes the body weight (kg), *age* corresponds to the age (years), and *gender* is +1 for females and −1 for males.

For gender and age groups, individual-specific average V_E values were summarized across individuals for four activity categories, including (1) sedentary and passive activities ($METS \leq 1.5$—including sleep or nap); (2) light intensity activities ($1.5 < METS \leq 3.0$); moderate intensity activities ($3.0 < METS < 6.0$); and high intensity activities ($METS > 6.0$).

Ambient nitrogen dioxide monitoring

Average hourly NO_2 concentrations considered as a marker for traffic pollution (14) were obtained from four Environmental Protection Ministry's online monitoring stations in Isfahan city, during winter 2014 to spring 2015. Two periods (winter and spring) were considered for calculating hourly NO_2 concentrations for holidays and school days.

Statistical analysis

Cosinor rhythmometry procedure is a statistical method that is widely used by scientists (15). In this study, three rhythm parameters including rhythm-adjusted mean level (mesor, *M*), half of the difference between maximums (amplitude, *A*) and the time point in the cycle of highest amplitude (acrophase, *Φ*) were analysed. In order to reduce the interindividual variety before cosinor analysis, the ventilation rate and outdoor time spent from each five person were averaged. The following time-dependent cosine function was then fitted to the hourly five person averages.

$$y = M + A\cos\left(\frac{2\pi\,t}{\tau} + \Phi\right)$$

Where y is the variable (i.e., ventilation rate and outdoor time spent); t is the elapsed time, M is the mesor; A is the amplitude; τ is the period of the rhythm (2- hour period); and Φ is the acrophase. The residual sum of squares, a measure of the deviation of the cosinor fit from the original waveform, was calculated. An analysis of variance (ANOVA) with 2-level factorial design was used to examine the effect of age, gender, season and day on the rhythm parameters. Statistical analyses were performed by Minitab (Minitab 17.3.1, Minitab, Inc., NC).

RESULTS

Demographic characteristics and clinical variables of the respondents are shown in Table 1. Elementary boys had the longest sedentary time as well as most of the time-spent on vigorous activities. Generally, senior students spent more time on moderate activities, but less time on other two activity groups. Maximum daily average inhalation rate (23.47 L min^{-1}) was observed among elementary boys, whereas minimum average daily inhalation rate (5.70 L min^{-1}) belonged to elementary girls. It is apparent from Table1 that boys had higher ventilation rates compared to girls.

Indoor air pollution sources

Exposure to second-hand smoke (SHS) was 31% among children and adolescents. Cooking frequency was 11 times a week among households. Natural gas was the most widespread fuel used in Isfahan urban area for indoor heating and cooking.

Popular activities and locations among toddlers

Table 1 supplementary highlights popular activities and the average time assigned to them among children and adolescents. The results confirmed that school attendance was the greatest time-consuming event after sleep. The common activities among children, adolescents, girls and boys were play, social and religious activities, housework, personal hygiene and commuting, respectively. The most visited places were home and school (Table 2). Microenvironments related to transportation, including streets, alleys and motor vehicles received 147 minutes a day. Girls used motorized travel more than boys, while boys walked or chose the bicycle trip mode. Parks and mosques were among local destinations popular among students, particularly boys.

Analysis of circadian rhythms in inhalation rate, compared to air pollution

Variations of ventilation rate and outdoor time-spent are

Table 1. Characteristics of sampled population, exposure to second-hand smoke (SHS, %), sickness history (SH, %), body weight (BW, Kg), average daily time-spent (minutes), body weight adjusted oxygen consumption (VO_2/BW: L O2/kcal) and ventilation rate (L/min) for light (METS ≤ 1.5), low (1.5 < METS ≤ 3.0), mid or moderate (3.0 < METS < 6.0) and high (METS > 6.0) intensity activities as well as basal metabolic rates (MJ/day) and body weights (kg) for gender and age groups.

Group	Age	N	Exposure to SHS	SH	BW	Time-spent					VO_2/BW					Ventilation rate					BMR
						Light	Low	Mid	High	Total	Light	Low	Mid	High	Total	Light	Low	Mid	High	Total	
High school																					
Girl	15≤age<17	98	21	0	57.3	713	602	139	0	1440	0.004	0.007	0.017	-	0.006	5.0	11.0	27.0	-	9.3	6.1
Boy	15≤age<18	84	35	17	65.6	167	618	681	120	1440	0.004	0.008	0.018	0.027	0.007	5.9	13.0	32.5	46.8	11.6	7.5
Total	15≤age<18	182	28	8	61.1	440	610	410	60	1440	0.003	0.007	0.017	0.026	0.007	5.5	11.9	28.2	46.8	9.8	6.7
Elementary																					
Girl	10≤age<12	124	26	13	40.9	754	171	515	0	1440	0.005	0.009	0.021	-	0.007	4.9	10.3	23.7	-	9.0	5.2
Boy	10≤age<15	93	42	23	52.7	764	487	226	0	1440	0.004	0.009	0.019	-	0.008	5.6	12.2	30.5	-	11.3	6.7
Total	10≤age<15	217	34	18	45.9	759	329	370	0	1440	0.004	0.008	0.019	-	0.008	5.3	10.9	26.9	-	9.5	5.8
Total	10≤age<18	399	31	13	52.8	560	470	390	30	1440	0.004	0.008	0.019	0.027	0.007	5.4	11.4	27.4	46.8	9.7	6.2

Table 2. Ten most popular locations and average time (Minutes ± SD) allocated to them among children and adolescents.

	girls		boys	
	Elementary school	High school	Elementary school	High school
Personal residence-indoor	1052 ± 216	1101 ± 217	1016 ± 255	1044 ± 255
School	202 ± 34	321 ± 16	248 ± 68	325 ± 21
Other residence-indoor	129 ± 161	73 ± 126	111 ± 130	26 ± 69
Car/truck/van travel	72 ± 45	26 ± 37	19 ± 40	27 ± 43
School grounds	64 ± 14	48 ± 9	52 ± 30	50 ± 6
Sidewalk-street	36 ± 44	59 ± 56	71 ± 65	70 ± 46
Park	31 ± 57	16 ± 43	92 ± 132	42 ± 77
Alleys/district	25 ± 40	10 ± 28	64 ± 62	72 ± 66
Residence-outdoor	22 ± 46	5 ± 16	12 ± 36	26 ± 45
Mosques/ religious site	11 ± 34	11 ± 28	18 ± 63	34 ± 69

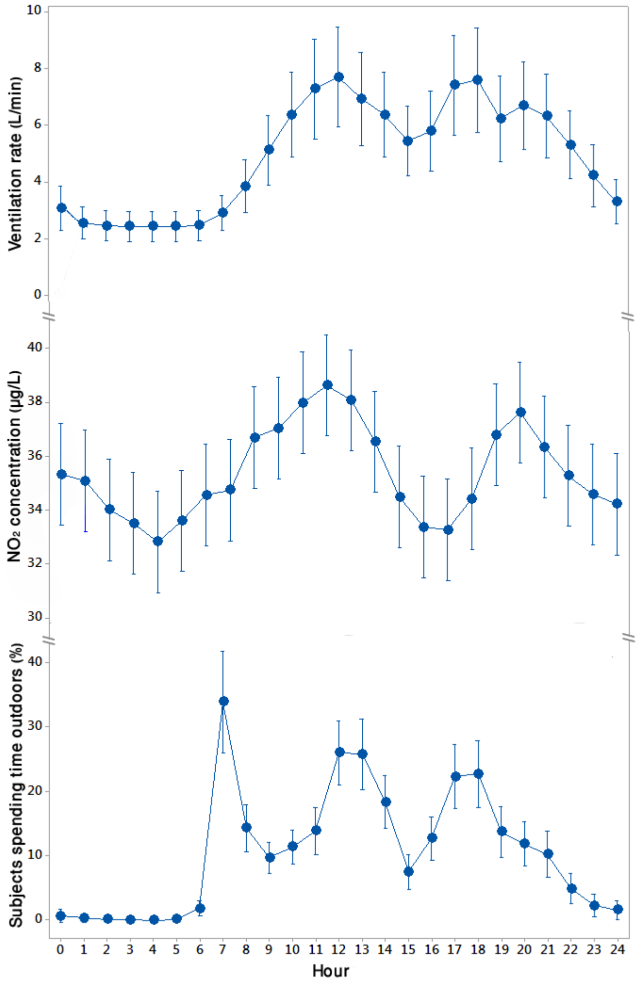

Figure 1. Diurnal variations of population outdoor time-spent, inhalation rate as well as concentrations of NO_2 in outdoor atmosphere of Isfahan city. Vertical bars indicate 95% confidence interval of the mean.

plotted on the same graph with variations of NO_2 pollution in the study area. It is apparent from Figure 1 that there is a significant circadian rhythm in air pollution and metabolic parameters (ANOVA, $p<0.05$). The circadian rhythm of ventilation rate was very similar to outdoor time-spent and outdoor air pollution.

In order to examine the effect of gender, age, season and day type, a factorial analysis compared rhythm parameters of mesor, amplitude and acrophase between male and female gender groups, child and adolescent age groups, spring and winter seasons and finally day types of school day and holiday (Table 3). The difference between gender groups and day types was significant among nearly all rhythmic parameters ($P < 0.01$), whereas age and season had no significant effects on circadian rhythm of outdoor time-spent and ventilation rate.

Figure 2 illustrates the 24-hour profile of population outdoors time-spent. Boys spent significantly (two-sample t-test, $P < 0.01$) more time outdoors than girls (182 ± 108 minutes vs. 140 ± 100 minutes, respectively). Daily pattern of outdoor time-spent varied across seasons and weekdays.

During school days, most of the outside time-spent by respondents was along the trip to school. Respondents spent on average 10-145 (69 ± 25) minutes a day on trip to school. A larger number of students spent winter mornings outdoors compared to spring mornings (Figure 2). Girls spent significantly (two-sample t-test, $P < 0.05$) more time outdoors in winter (149 ± 105 minutes/day) than in spring (123 ± 86 minutes/day). The reverse trend was true for boys (191 ± 113 in spring vs. 176 ± 104 in winter) but not significant.

In order to compare the findings from this study regarding the population groups with the highest risk of exposure to air pollution, health statistics, the respiratory and intrathoracic cancer incidence obtained from Iran's cancer report (16) were illustrated in Figure 3. The respiratory and intrathoracic cancer incidence was higher among female infants, but with increased age, this incidence was higher among male population (Figure 3).

DISCUSSION

Analysis of results showed increased pollution was concurrent with increased inhalation rate. There was a significant circadian rhythm in inhalation rate, outdoor time-spent and NO_2 pollution, indicating increased risk on particular hours during the day. This finding suggests that actual exposure levels may be underestimated when the simple risk assessment method is implemented without the use of activity-space-time data. Similarly, Shekarrizfard and Faghih-Imani (17) observed that personal exposure to NO_2 was more elevated than the exposure level calculated based on NO_2 concentrations at home location.

Inhalation rate was higher among boys compared to girls and even more elevated among elementary students than high school adolescents. Therefore, elementary boys may be at higher risk of exposure to air pollution. Boys spent more time outdoors and in traffic than girls. Besides, they used active modes of transport like walking and cycling. These facts prove that boys were exposed to outdoor air pollution more than girls. Similarly, Zeng and Qian (18) found that Chinese boys (5-17 years old) were more sensitive to NO_2 than girls. Several epidemiologic studies have found a stronger negative association between air pollutants and health effects among small children compared to older ones (19).

Higher exposure to air pollution among elementary boys makes them more susceptible to health hazards from air pollution. Iran cancer statistics (16) were consistent with our findings. While respiratory and intrathoracic cancer incidence was smaller among newborn boys, it surpassed the girls cancer incidence after the age of 15 and continued increasing exponentially. Accordingly, higher exposure in boys may account for the larger cancer incidence after a time lag.

Indoor and outdoor time budget of an individual has a significant relevance to his or her exposure to air pollution, because of difference in pollution level between these two microenvironments, especially in the heating season. Respondents spent 89% of their time inside and 82% of their inside time at home. Similarly, urban Canadian adolescents (12-19 years old) spent 21.8 hours indoors, 16.7 hours at home and 0.8 hour in the vehicle (20). As a result, outdoor pollutant concentrations may not be a good proxy for population exposure to air pollution.

Table 3. F values resulted from factorial analysis of variance for rhythm parameters of the cosinor analysis for outdoor time-spent and ventilation rate.

Source	df	Outdoor time-spent			Ventilation rate		
		Mesor	Amplitude	Acrophase	Mesor	Amplitude	Acrophase
Linear	4	8.26**	1.66	11.36**	922.86**	176.30**	15.65**
Gender	1	8.71**	0.54	0.25	32.02**	4.74*	0.04
Grade	1	0.45	1.73	0.01	1.00	0.21	0.04
Season	1	0.02	1.97	0.13	0.26	2.16	1.73
Day	1	9.15**	2.20	21.69**	1916.47**	336.13**	32.00**
2-Way Interactions	6	1.52	3.16**	5.41**	9.01**	3.69	0.52
Gender*grade	1	9.94	0.00	0.14	0.31	0.73	0.16
Gender*season	1	0.56	0.71	0.01	7.86**	1.88	0.04
Gender*day	1	1.73	8.48**	6.21*	14.62**	6.17	0.23
Grade*season	1	0.01	0.00	2.05	0.07	0.10	0.28
Grade*day	1	0.09	0.29	3.83*	0.03	0.06	0.05
Season*day	1	0.11	1.43	4.97*	2.53	0.56	1.03
3-way interactions	4	0.86	1.88	0.43	3.09*	1.56	0.06
Gender*grade*season	1	0.88	0.00	0.27	1.07	0.39	0.00
Gender*grade*day	1	0.15	0.54	0.02	0.30	2.60	0.01
Gender*season*day	1	0.34	4.52*	0.18	2.01	3.57*	0.08
Grade*season*day	1	0.16	0.47	0.37	2.32	0.07	0.04

* significant at P < 0.05 level
** significant at P < 0.01 level

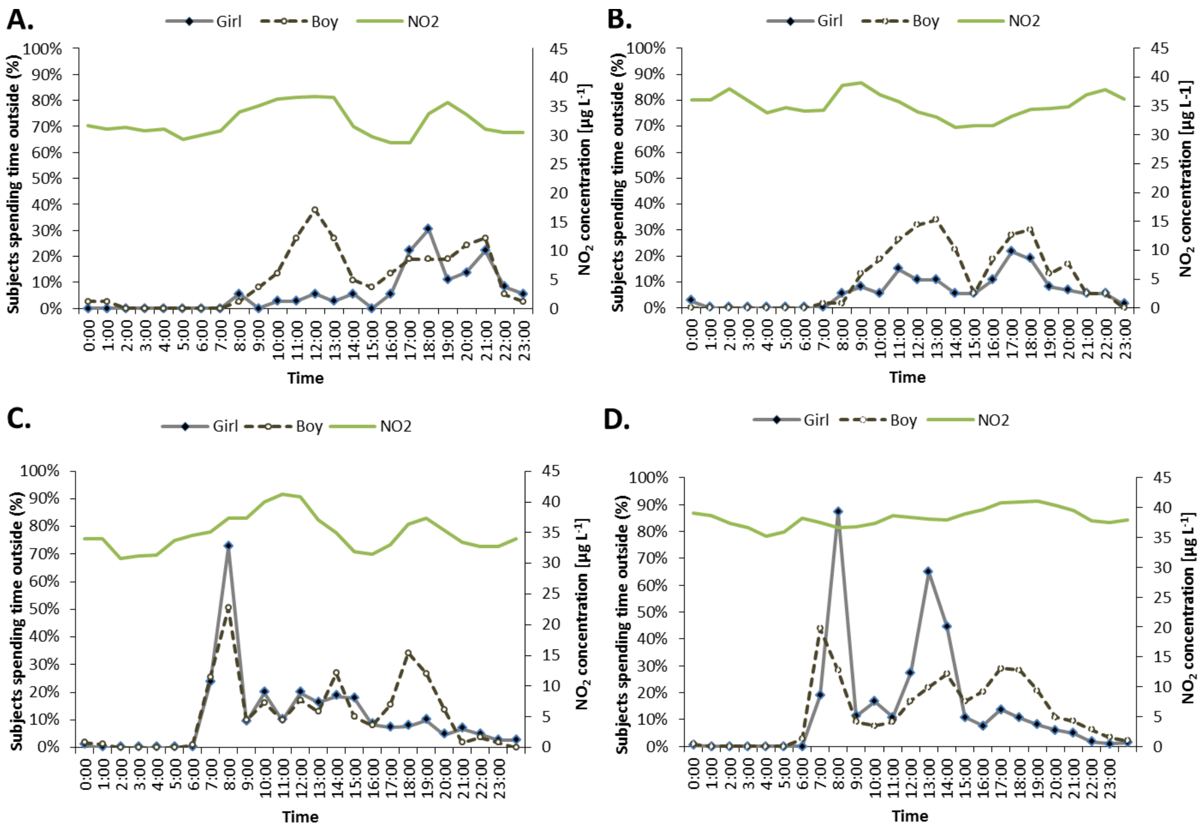

Figure 2. Diurnal variations of the percent of respondents spending time outdoors (primary vertical axis) and NO_2 concentration (µg L^{-1}) on A. Spring, and B. Winter school days, as well as on C. Spring and D. Winter holidays.

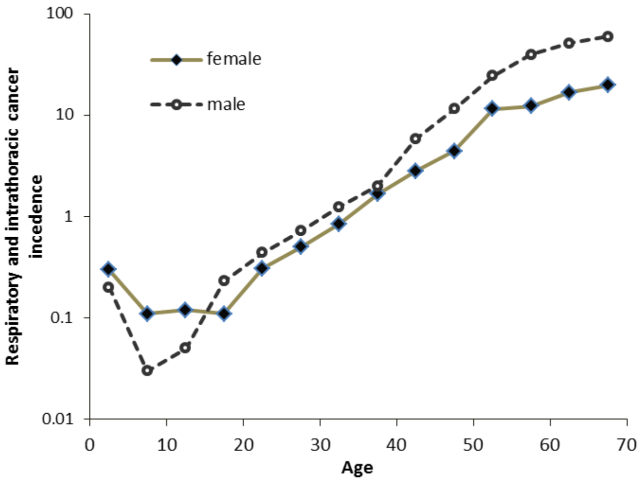

Figure 3. Respiratory and intrathoracic cancer incidence among female and male population for age intervals. Data obtained from Iran's cancer report.

Children and adolescents also spent a significant amount of their time in school during the highly polluted hours of the day. Thus, the air quality of this indoor microenvironment may affect the child's exposure level.

Major indoor pollution sources at home location included smoking, cooking and cold season heating. Researchers have estimated that the contribution of indoor $PM_{2.5}$ sources to total child exposure was 75% (5). The percent of population exposed to second-hand smoke was 30%. It was less than the value of 38.6% obtained from another Iranian study (21), and it was similar to other countries such as Scotland, 31% (22), United States, 25% (23), and China, 48% (24). Although children and adolescents spent a small portion of their indoor time in the kitchen, exposure to cooking generated pollutants could be significant, due to the air exchange between kitchen and bedroom (5). Furthermore, almost all Isfahanian population used natural gas as the main fuel, except for less than 0.15% that used solid fuels for cooking and indoor heating (25).

Outdoor air pollution, particularly in cold season was significantly higher than indoor air pollution in the study area (26). During school days, much of the outside time-spent (10-145 minutes) by respondents was along the trip to school. This finding was consistent with past studies on English students who spent 15-180 minutes on trip to and from school (11). The contribution of this trip to total exposure could be very elevated because of the higher energy expenditure and consequently, higher inhalation rate during this trip among students. In another study, commuting and out-of-home activities were responsible for 23-44% of an individual's exposure to air pollution (17). In addition, girls used motorized travel more than boys, while boys walked or chose the bicycle trip mode. This may account for_inequality in exposure level among gender groups as research showed that there was a hierarchy of pollutant concentrations in roads, buses, cars and underground trans (27)._Parks and mosques were among local destinations popular among students, particularly boys.

CONCLUSION

Increased NO_2 pollution was concurrent with the increased inhalation rate among children and adolescents. In addition, elementary children and boys were at higher risk of exposure to air pollution. Locations associated with the highest exposure like home, school and transportation need to be taken into account for effective environmental risk management. This study contributes to the environmental risk assessment literature by showing that spatiotemporal variability of daily activities should be taken into account for accurate health risk assessments.

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