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Association between Urban Benzene Pollution and Incidence of Acute Myeloid Leukemia

Maryam Massaeli[1], Abdulrahman Bahrami[2], Masoud Shahabian[3*]

[1]Assistant Professor, Emergency Medicine Department, AJA University of Medical Sciences, Tehran, Iran
[2]Professor, Occupational Health Department, Hamedan University of Medical Sciences, Hamedan, Iran
[3]Resident, Emergency Medicine Department, AJA University of Medical Sciences, Tehran, Iran

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*Corresponding author:
Masoud Shahabian,
Resident, Emergency Medicine Department, AJA University of Medical Sciences, Tehran, Iran
Tel: +98 915 5200856
Email: elmpajooh@yahoo.com,
ORCID: 0000-0001-9345-5589

ABSTRACT

Background: Benzene has been classified as group 1 human carcinogens in the environment by the International Agency for Research on Cancer (IARC) mainly because of its ability to cause acute myeloid leukemia (AML). This study was conducted to detect any probable association between urban benzene pollution concentration and occurrence of AML in different regions of Tehran.
Methods: In this descriptive study, demographic data of AML cases recorded in cancer registry centers of Tehran city since March 2006-2011 who met the inclusion criteria were extracted. Eligible criteria included residing in Tehran city for at least 5 years prior to diagnosis of AML. Collected data were correlated with concentration of benzene in ambient air available since March 2001 to March 2011.
Results: The majority of AML subjects were male in the age range of 20-30 years. Maximum concentration of benzene was reported from southern (11.35-106.57 ppb) and central (5.5-60.18ppb) regions of Tehran. The association between benzene concentration with occurrence of AML was observed significant for the period between March 2010 to March 2011 for male patients (Pearson correlation=0.906, P=0.05) in the age range of 30-40 years (Pearson correlation=0.893, P=0.041).
Conclusion: This study suggested probable evidence for the association between the incidence of AML and concentration of benzene in southern and central areas of Tehran city.

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Introduction

AML is a hematologic malignancy which needs urgent diagnosis and aggressive treatment. Otherwise it causes bone marrow failure and death.[1] AML is plausibly related to genetic disorders, radiation exposure, chemotherapeutic agents, viruses and could be related to exposure to physical and chemical substances such as benzene.[2] International Agency for Research on Cancer (IARC) has classified benzene as a group 1 human carcinogen.[3]

Benzene is a colorless to pale yellow liquid with an aromatic odor. This chemical compound enters the human body through inhalation, ingestion and skin contact and after entering the bloodstream, due to the lipophilic properties, is distributed in the body depending on the fat content of the organs.[4] Benzene is a component of crude oil and gasoline fuels[5] and is a commonly used solvent in multiple industries specifically in the production of plastics and rubber.[6] Cigarette smoking can also increase exposure to benzene which is present in the tobacco smoke.[7] Transportation is contributed to be responsible for 85% of benzene in the atmosphere.[8] Benzene concentration in the ambient air of urban areas is generally higher than other areas. Benzene is present in the ambient air as a result of reactions such as combustion

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of fuels and indoor environments because of cooking and heating.[5] Benzene exposure also occurs at time of refueling automobiles.[8, 9] Repeated exposure to benzene in various environments has caused serious concerns regarding the health of general population mainly because of its hematotoxic effects in levels as low as < 1 ppm.[3] Damage to the immune system, menstrual disorders, and changes in ovarian size are some of the other complications caused by exposure to benzene.[10] The most common route of exposure to benzene is inhalation and it has been indicated that 0.02, 0.015, and 70 µg of benzene is absorbed by humans daily through food, water and ambient air, respectively.[4]

European Union and North American countries have agreed on the range of 0.5-1 ppm for occupational exposure to benzene.[11] The concentration of benzene in the ambient air varies from 0.2 µg/m^{-3} in rural areas to 349 µg/m^{-3} in the center of industrial areas with heavy traffic.[4] Numerous studies over the years have described a significant association between occupational exposure to benzene and development of acute leukemia.[12, 13] The national standard amount of benzene in the ambient air in Iran is reported to be 1.5 ppb.[14] The study conducted by Bahrami et al. showed that the average concentration of benzene measured in the ambient air of Tehran was 127.6 ppb.[15] He attributed the major hydrocarbon pollution in the ambient air of Tehran to the transportation source. There is enough evidence for this claim since a dramatic increase in the number of vehicles in Iran was observed from 100 in 2004 to 251 in 2011 per 1000 populations.[16] In a study conducted by Wolff in UK, there was a correlation between AML incidence and number of the cars.[17] In another study carried out in the Illawarra region of New South Wales, in spite of very low concentrations of benzene in the ambient air, an increase in cases of leukemia among children was reported.[18] Crosignani et al. assessed the effect of road traffic on the risk of childhood leukemia in northern Italy and found a significant difference between children whose home was not exposed to road traffic emissions comparing with heavily exposed children.[19]

Raaschou-Nielsen et al. showed that risk of leukemia increased by 25% in children whose mothers had exposed to benzene during pregnancy.[20]

To the best of our knowledge, there is no study assessing the association between benzene concentration in the ambient air and incidence of AML in the context of a population-based study in Iran. We aimed to investigate the frequency of leukemia in relation to the concentration of benzene in the air of urban regions of Tehran.

Materials and Methods

The study was a descriptive analysis of data corresponding to all patients with AML recorded in cancer registry centers of Tehran city (Imam Reza Hospital, Shariati Hospital, Imam Khomeini Hospital, and Iran Cancer Institute) from March 2006 to March 2012. The study protocol was reviewed and approved by Ethics Committees of Shahid Beheshti University of Medical Sciences, Tehran (Number: IR.AJAuMS.REC.1390.10). Eligible criteria included residing in Tehran for at least 5 years prior to diagnosis of AML. Total number of AML cases found in cancer registries was 338 that based on study criteria, information of 319 patients were extracted from their records. Patients were classified into eight age groups with 10-year intervals starting from less than 20 years to more than 80 years of age.

To study the relationship between benzene concentration and incidence of AML, Tehran was divided into 5 regions including north, south, east, west and central regions. At first, patients were coded according to their place of residence, age and sex. Then, according to each person's address, and using the map of Tehran, the distance of the patient was determined from the sites where concentrations of benzene were recorded. To obtain benzene concentration values from March 2001 to March 2012, two sources of information including Tehran Air Quality Control Organization and measurement records reported in the literature were used. Data were analyzed by SPSS using one-way analysis of variance, Pearson correlation and regression analysis and presented as mean values. P value=0.05 was considered statistically significant.

Results

Patients Characteristics

The sample consisted of 223 (69.9%) males, and 96 (30.1%) females. The average age of the patients was 49.93±19.76 years, ranging from 16 to 93 years with Skewness coefficient of 0.007. The lowest number of AML patients belonged to the group of patients less than 20 years (8 male and 5 female). The number of male patients in the second group (between 20 and 30 years) was higher than other age groups (n=49). 22.91% of female patients were in the range of 50-60 years (n=22). Distribution of patients in five regions of Tehran identified 77 (24.1%), 72 (22.6%), 69 (21.6%), 67 (21%), and 34 (10.7%) cases of AML who belonged to the central, northern, southern, eastern, and western areas of Tehran, respectively. Figure 1 exhibits gender distribution of patients in different regions of Tehran.

Benzene Concentrations in Inhaled Air

Figure 2 shows the values of benzene concentration in different regions of Tehran at four time periods including years 2001-2002,2009-2010 ,2006-2007 , and 2010-2011. The highest concentrations of benzene in the inhaled air were recorded in center and south of Tehran in time intervals of 2001-2002 and 2006-2007, respectively. At a four-year interval, concentration of benzene in the ambient air was reduced from 60.18, 34.48, 106.57, 48.58, and 47.01 ppb to 5.5, 1, 11.35, 2, and 2.43 ppb in the center, north, south, east, and west of the city, respectively. Table 1 provides the correlation between benzene concentration and incidence of AML measured in different years which the most significant association (0.838) was observed in the period since March 2006 to March 2007 and also March 2009 to March 2010.

The Relation between Benzene and AML

Table 2 expresses the level of correlation between

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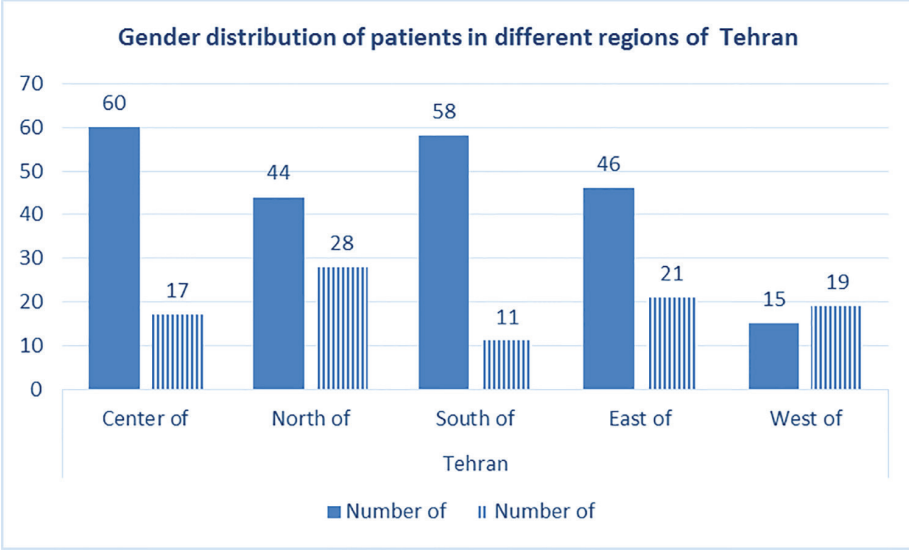


Figure 1: Gender distribution of patients in different regions of Tehran

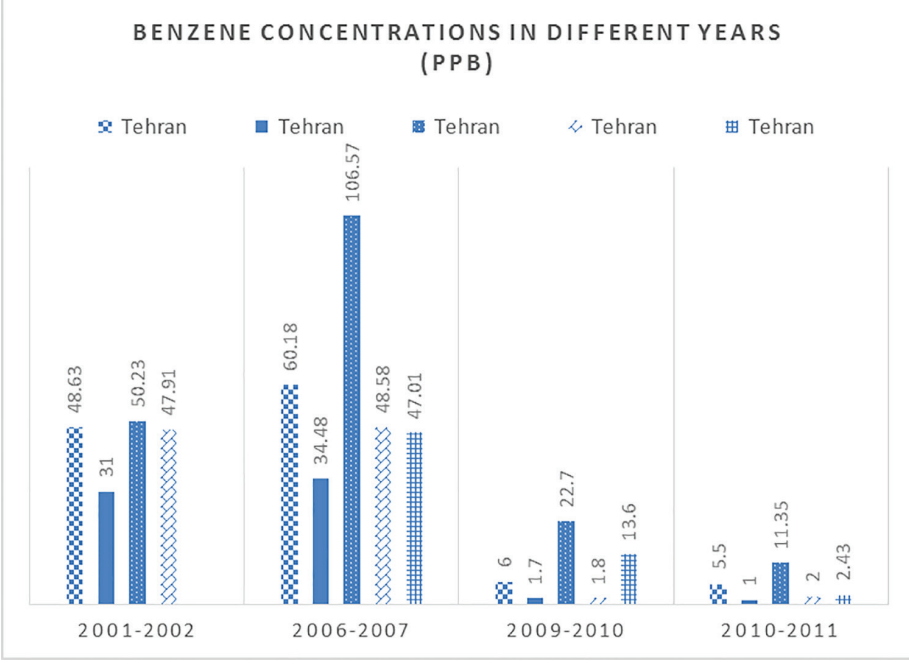


Figure 2: Mean values of benzene concentration in different regions of Tehran city at various years

Table 1: Correlation between benzene concentration and incidence of AML measured in different studied years

Studied years		Incidence of AML			
		2010-11	**2009-10**	**2006-7**	**2001-2**
2010-11	Pearson Correlation	1	0.161	0.410	0.576
	P value		0.796	0.493	0.424
2009-10	Pearson Correlation	0.161	1	0.838	0.479
	P value	0.796		0.077	0.521
2006-7	Pearson Correlation	0.410	0.838	1	0.679
	P value	0.493	0.077		0.321
2001-2	Pearson Correlation	0.576	0.479	0.679	1
	P value	0.424	0.521	0.321	

benzene concentration and AML in both genders in studied years. It shows the Pearson coefficient of 0.906 at significance level of P=0.05 for the correlation between benzene concentration and men with AML in the last year of study, while does not reveal any correlation between females with AML and benzene concentration in any studied period.

Correlation between benzene concentrations in different age groups was also determined (Table 3). A significant correlation between benzene concentration and incidence

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Table 2: Correlation of benzene concentration with risk of AML based

Gender	Statistics	With Benzene Concentrations			
		2010-11	2009-10	2006-7	2001-2
Male	Pearson Correlation	0.906	0.634	0.726	0.702
	P value	0.05	0.366	0.276	0.298
Female	Pearson Correlation	-0.559	-0.828	-0.905	-0.874
	P value	0.327	0.084	0.034	0.126

Table 3: Correlation of benzene concentrations with risk of AML based on age groups

Age range (years)	Statistics	With Benzene Concentrations			
		2010-11	2009-10	2006-7	2001-2
<20	Pearson Correlation	-0.052	-0.550	-0.363	-0.945
	P value	0.934	0.337	0.548	0.055
20-30	Pearson Correlation	0.698	0.109	0.579	0.627
	P value	0.190	0.861	0.307	0.373
30-40	Pearson Correlation	0.893	-0.186	0.096	0.532
	P value	0.041	0.764	0.912	0.468
40-50	Pearson Correlation	0.293	-0.830	-0.572	-0.481
	P value	0.633	0.082	0.313	0.519
50-60	Pearson Correlation	0.295	0.180	0.426	-0.304
	P value	0.630	0.772	0.475	0.696
60-70	Pearson Correlation	0.007	-0.641	-0.153	-0.260
	P value	0.991	0.244	0.806	0.740
70-80	Pearson Correlation	0.456	-0.001	0.366	-0.256
	P value	0.440	0.998	0.544	0.744
>80	Pearson Correlation	0.161	0.098	0.023	0.823
	P value	0.796	0.875	0.971	0.177

of AML in the group of 30-40 years in the last year of study was observed (Pearson coefficient=0.893, P=0.041). The next remarkable correlation belonged to the benzene concentration and patients with AML older than 80 years in the first year of study (Pearson coefficient=0.823, P=0.177).

Discussion

Results indicated a remarkable difference between concentrations of benzene in different regions of the city and with incidence of AML as well. Previous studies have shown that emission of hydrocarbons in south of Tehran exceeds that in the north of the city. Hence, high concentrations of benzene in the central and southern regions of the city can be attributed to vehicle density in these districts. Geographical parameters also play an important role in pollution conditions.[15] These effects were observed in the difference between pollutant concentrations among different regions of Tehran. According to the results, benzene concentrations in northern part of the city were strongly lower than other districts of the city which could be due to higher altitude of this area compared to other regions of the city. Furthermore, the direction of the wind in Tehran is from west to the east that impacts the concentration of the pollutants.

The difference of benzene concentrations in the ambient air between the first and last years of the study can be explained by higher rate of worn out vehicles that transited in the time interval of 2001-2002 compared to 2010-2011 when the average age of vehicles in Iran was reduced from 20 years to 13 years. In addition, during these years, vehicles with new technologies equipped with return catalyst system replaced the older ones and the amount of benzene in petrol was reduced in 2010-2011 compared to previous years.

Information related to values of benzene concentration in various regions of the city in different years showed that 94.7% of these values were higher than permitted levels of exposure in the ambient air (1.5 ppb). Literature review is in concordance with the findings that values of benzene concentration in the air of the gas stations or industrial environments, where concentrations exceeded the permitted limits, were associated with increased occurrence of leukemia[21-23] and changes in hematological parameters.[24] Collins et al. (2003) study regarding the investigation of lymphohematopoietic cancer mortality among workers with benzene exposure showed increased rates of acute non-lymphocytic leukemias and multiple myeloma at benzene concentrations greater than permitted levels of occupational exposure.[25]

In this study, no clear evidence was found for an association between benzene concentration in the ambient air and incidence of AML in females, while AML development in men was related to the urban benzene pollution. These results contradict the results of the study of Visser et al. (2004) where an association was reported between residential traffic intensity as a source of benzene pollution with occurrence of hematological malignancies only in females and not in males.[26] No information was available regarding the patients' jobs, hours of their activity outside the home

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or patients smoking habits. Hence, it was not possible to differentiate between patients of different ages and genders in relation to levels of their exposure to benzene with the purpose of attributing more incidence of AML among men to the factors such as more exposure of them to benzene in comparison to women. The differences in the incidence of AML by age and sex could result from effect of physiological differences between patients' sexes and various categories of ages on pharmacokinetic (absorption, distribution, metabolism, elimination) of a solvent such as benzene.[2] Furthermore, genetic factors and family history are known for their roles in the risk of AML, although they plausibly account for less than 10% of overall risk.[27] According to the evidence provided by some studies, obesity and dietary factors are also associated with increased risk of AML.[28, 29]

Conclusion

In summary, findings of this study demonstrated an association between benzene concentrations in the ambient air of Tehran an increased risk of AML, especially in the southern and central regions of Tehran city. Benzene exposure of men at the ages between 30 and 40 years was associated with the development of AML, while no association was found between benzene exposure and female cases of AML.

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Conflict of Interest: None declared.

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