

Research Paper Estimation of Epidemiological Indicators of Long-term Exposure to PM_{2.5} and Its Impact on Lung Cancer in People Over 30 Years in 2008-2017 in Ahvaz City, Iran

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ABSTRACT

Background & Aims of the Study: Lung cancer is one of the most common cancers globally and the third leading cause of death in Iran. Particulate matter is one of the leading air pollutants in urban areas that can pass through the nose and throat, penetrate deep into the lungs, and cause serious health outcomes. Our primary purpose was to estimate the rate of lung cancer deaths in people over 30 years of age in the long-term exposure to PM_{2.5} in ten years in Ahvaz.

Materials and Methods: Data related to deaths (including population and incidence of health outcomes) and $PM_{2.5}$ were obtained from the Deputy of Health, Environmental Protection, and Meteorological Organizations of Ahvaz. After validating the data according to Aphekom's instructions, they entered the AirQ+ software. Also, 24-hour particle concentrations during the year, total population, at-risk population, the baseline incidence rate of desired health outcomes, and particle threshold of $10\mu g /m^3$ were prepared and entered into the software.

Results: The highest concentration of $PM_{2.5}$ was in 2010 (70.72 µg/m³), and the lowest concentration was in 2014 (41.97 µg/m³), and in all years of measurement, the amount of $PM_{2.5}$ was higher than the WHO standard (10 µg/m³). The results showed a significant relationship between lung cancer and $PM_{2.5}$ concentration. Thus, with the increase of air pollution in Ahvaz due to $PM_{2.5}$ pollutants, mortality and the risk of these diseases increased. The results obtained for mortality due to lung cancer is one of the most deadly types, had the highest attributable 28.57% (2010) and the lowest 20.63% (2014). Also, the highest and lowest total attributable individuals were 24 (2010) and 18 (2014), respectively. Thus, $PM_{2.5}$ pollutants can be effective in people with lung cancer.

Conclusion: As we know, this pollutant has caused many destructive effects and mortality to the residents of Ahvaz. For this purpose, the authorities in this field must provide preventive and applicable solutions to reduce the concentration of particulate matter and investigate the impacts. It can be concluded that appropriate measures and policies should be adopted to reduce air pollution in controlling $PM_{2.5}$ sources of pollution to reduce the health effects of this pollutant in urban residents. Accordingly, it has been proven that reducing air pollution can reduce the burden of lung cancer and acute and chronic respiratory diseases. According to studies, a decrease of 10 m³ in the concentration of particulate matter $PM_{2.5}$ increases life expectancy by about 0.61 years.



1. Introduction

articulate matter affects people more than any other type of air pollutant. The main constituents of particulate matter are sulfates, nitrates, ammonium, sodium chloride, carbon black, mineral particles, and water. In other words, particulate matter is

a complex mixture of solid and liquid particles composed of particulate organic and inorganic matter. Chronic exposure to particulate matter causes lung disease as well as lung cancer. Lung cancer remains the leading cause of cancer death in the world. The metal compounds of PM, especially the metals in PM25, are often considered the most important factors affecting people's health. These compounds are usually emitted from metal-related processes, resulting in impurities and contaminants in fuels and non-exhaust emissions (due to vehicles' corrosion and wear and tear) [1]. Intermediate metals, such as iron, vanadium, nickel, chromium, and copper have always been considered because of their potential to produce reactive oxygen species (ROS) in biological tissues. The mode of action of metals with oxidation-reduction properties is that the intermediate metals in the d orbital have non-coupled electrons and can produce free radical species with biological reducing factors and through oxidation-reduction mechanisms. Various studies have been performed on the health impacts of PM heavy metals in different parts of the world. However, due to the contradictions, the role of each specific source in creating health impacts cannot be clearly stated.

The role of copper and lead in monthly mortality has been confirmed using experiments. Also, the relationship between blood lead levels and mortality of CVDs has been proven. Aluminum and silica levels are strongly related to the dispersion and suspension of soil particles and are predicted to have the least effect on daily mortality. Studies on the role of PM metal compounds in mortality have reported a significant relationship between iron, zinc, and nickel in PM25 on the one hand and between magnesium and zinc in PM₁₀ on the other hand with mortality. Particulate matter respiration test using healthy volunteers showed that inflammation and increased blood fibrinogen were associated with Fe /Se /Sulphate and Cu /Zn /V, respectively. The particulate matter respiration test using healthy volunteers showed that inflammation and increased blood fibrinogen were associated with sulfate levels, but no significant association was found with cadmium, potassium, zinc, calcium, and nickel, respectively. A study in the Utah Valley looked at the impact of PM on people during the operation of a steel plant and the closure of the plant and found

that lung damage and pneumonia increased during the operation of the steel plant.

Particulate matter experiments during this period showed that the concentrations of iron, copper, nickel, zinc, and lead in the particles increased, which could be a reason for high biological activity. In addition, in vitro studies have shown that during the operation of the steel plant, the capacity to produce oxygen radicals in the cells increases, and the release of cytokines intensifies. Another study in Eastern Europe reported that inflammatory impacts were exacerbated by high concentrations of zinc, copper, nickel, and calcium PM compared to their low concentrations in healthy volunteers. Vanadium and chromium (not iron, nickel, copper, and platinum) in PM_{2.5} particulate matter have also been reported to increase oxidative stress as well as DNA damage [2].

Prolonged exposure to particulate matter can cause a wide range of epigenetic changes, and many epigenetic changes play an important role in the carcinogenesis of lung cancer in the United States. Lung cancer has been on the rise in China since the mid-1960s, increasing exposure to particulate matter. Also, if the concentration of these pollutants decreases, if other factors are constant, the deaths attributable to it will decrease, and this indicates that if the concentration of particulate matter decreases, the community's level of health can be improved. It should be noted that some researchers have observed the health impacts of particulate matter even at very low concentrations; this means that there is no threshold below which no adverse effects can be observed for particulate matter [3, 4].

The World Health Organization (WHO) estimates that if the world average annual PM₁₀ concentration falls below the current level of 70 μ g/m³ to the target level of 20 μ g/m³, the attributable mortality rate will be reduced by about 15%. Numerous studies have shown that exposure to particulate matter is associated with health impacts, such as respiratory diseases. As shown in Figure 1, the rate of precipitation of particulate matter in different areas of the respiratory system depends on the size of the particulate matter, and their impacts will become more and more severe as the particle size decreases. Researchers have shown that PM10 is associated with hospitalization for respiratory diseases. PM25 has also been strongly associated with respiratory diseases and lung cancer. Very fine particulate matter PM₁₀ penetrates the lower parts of the respiratory system and into the lungs' alveoli, causing numerous respiratory attacks [3].



Figure 1 compares the precipitation of particles inhaled through the mouth and nose into the lungs' air sacs. For oral respiration, the particle size, from which the smaller particles began to penetrate inside and precipitated in the lungs is approximately 10 μ m. Coarse particles are either unable to enter the airways or are removed in the upper respiratory tract by inertial collisions and gravity separation. Precipitation in the lungs increases by approximately 50% for particles of 2.5 μ m. As the particle size decreases to less than 2.5 μ m, precipitation in the lungs decreases due to the decreasing trend of inertial collisions.

The minimum precipitation occurs at approximately 0.2 to 0.4 μ m. It should be noted that high-efficiency air pollution control devices are also the least efficient in this size range. The lack of effective collection mechanisms in this area and their presence in the human environment causes these particles to be inhaled into the body; fortunately, only a tiny part of them is precipitated, and most of them are excreted during exhalation. Precipitation of smaller particles of 0.2 µm begins to increase again, and this is due to the increased effect of the Brownian diffusion of the particles. The modernization and industrialization of countries have been accompanied by the production of gases and polluted particulate matter in the air, which leaves no room for breathing, and has made the inhalation of clean air, which has always been the joy of human life, an unattainable dream. Global statistics also show that about 4.5 million people die each year due to air pollution [4].

In Iran, 2,527 people have lost their lives due to air pollution, while 2,522 cardiac patients and 4,525 respiratory patients are hospitalized simultaneously for air pollution [5]. Published results from the latest research by the WHO and the International Agency for Research on Cancer (IARC) also provide us with a newer reality in this area. The results tell us that in 2010, about 223,000 people worldwide died of lung cancer, more than half of them from East Asia and China. Earlier, the IARC reported some particulate matter, such as diesel smoke, as carcinogenic, but this new report identifies all compounds in air pollution as carcinogenic. The agency also reported an increase of $10 \,\mu g /m^3 PM_{2.5}$ resulted in a 14% increase in lung cancer, a 6% increase in deaths, and a 12% increase in cardiovascular disease. The IARC has identified particulate matter as Group 1 carcinogen for humans [6-11].

Exposure to PM_{2.5} and lung cancer mortality were examined in Polish cities from 2006 to 2011. The results showed that the average annual concentration of PM₂, varies from 14.3 to 52.5 µg /m3. Also, the average population attributable to this pollutant for lung cancer ranged from 0.195 to 0.413. Another study looked at estimates of premature deaths from PM25 exposure and the benefits of China's air pollution control policies for 2020. The rate of premature death was very high in densely populated cities, such as Shanghai (18,679 people per year), Chongqing (23,561 people per year), and Beijing (18,817 people per year). Among all deaths, the share of lung cancer was 45% [12]. In recent years, various agencies have developed various tools to assess the health impacts (HIA) of air pollution, including AirQ, BenMAP, Aphekom, and AirQ+. The AirQ+ modeling software was developed by the WHO (WHO) to assess the Health Impacts (HIA) of short- and long-term exposure to indoor and outdoor air pollution and includes the relative risk functions, attributable component, and some attributable cases reported in recent epidemiological studies [13-16].





Figure 1. Comparison of particulate matter precipitation in the pulmonary region through the mouth and nose breathing [3]





Figure 2. Geographical location of the study area [18]

According to the list of the most polluted cities in the world, Ahvaz in Iran, Olanbatar in Mongolia, Sanandaj in Iran, Ludhiana in India, Quetta in Pakistan, Kermanshah in Iran, Peshawar in Pakistan, Gaborone in Botswana, Yasuj in Iran, and Kanpur in India are the ten most polluted cities in the world, respectively. In other words, Ahvaz has been declared the first polluted city globally, Sanandaj the third polluted city, Kermanshah the sixth polluted city, and Yasuj the ninth polluted city globally [17]. Therefore, the purpose of this article was to analyze the association between lung cancer in people over 30 years of age attributable to PM_{2.5} pollutants using the AirQ+ model in Ahvaz from 2008 to 2017.

2. Method

This study evaluated the number of deaths (per 100,000 population), including lung cancer in adults over 30 years of age attributable to $PM_{2.5}$ exposure in Ahvaz (2008-2014). The city of Ahvaz, with an area of 18,650 hectares, and a population of approximately 1.3 million people, is considered one of the largest cities in Iran (the fourth largest city in Iran). The city is located 31 degrees and 20 minutes north and 48 degrees and 40 minutes east [18]. The geographical location of the study area (Ahvaz city) is shown in Figure 2.

Data related to deaths were collected from the Deputy of Health of Ahvaz. Also, $PM_{2.5}$ pollutant data were taken from environmental protection and meteorological organizations of Ahvaz to determine the air pollution,



and after eliminating the zero and negative values, according to Aphekom criteria, the measure was taken to estimate the epidemiological indicators [19]. Then, by entering $PM_{2.5}$ pollutant data into AirQ+ software, the relationship between lung cancer and $PM_{2.5}$ pollutant in the structure of Ahvaz city was analyzed. Population contact data, including population, lung cancer incidence, and air quality data, were entered into the software. In Equation 1, RR was used to calculate the value of AP [20].

$$1. AP = SUM \frac{\{[RR(c)-1] \times P(c)\}}{SUM[RR(c) \times P(c)])}$$

Where, AP is equal to the proportion of the population exposed to the contaminant over a specified period (Attributable Proportion), RR (c) is the relative risk of health impacts on the target population in the contact category c (Equation 2), and P (c) is the population proportion of the exposure group. After calculating the amount of AP, with the help of Generalized Linear Models (GLM) and Generalized Additive Models (GAM), the amount of damage to health in 100,000 sections of the basic population was calculated. RR is a selective health outcome using contact-response functions derived from epidemiological studies. We used the default RR values in the AirQ+ model (Equation 2).

2. $RR(X) = e^{\beta(X-X)}$

In this formula, X, X0, and β indicate the average concentration of PM_{2.5} in Ahvaz. The number of attributable cases to 100,000 people at risk (BE) knowing the base-

line incidence of selective health outcome (B) in the target population can be calculated with Equation 3.

3. $BE=B \times AP$

B indicates the number of health outcomes per 100,000 at-risk Population. Due To The Inability To Access Hospital Data, Baseline Incidence (BI) values were used in other studies [13, 20, 21]. Finally, the total number of attributable cases (NE) was calculated to evaluate the health impacts on the number of at-risk populations (N) using Equation 4.

4. $NE = BE \times N$

For statistical analysis, after collecting information and data, SPSS, R, and Minitab software was used for editing and formulation in Excel software in VBA language and analysis. The Kolmogorov-Smirnov test was used to check the normality of the data distribution. The ANO-VA was used to compare the mean concentration of $PM_{2.5}$. To calculate the AP (according to the variety of stations and Spatio-temporal fluctuations), the location of the stations was determined, and then, the health effects of $PM_{2.5}$ were determined in ten years in Ahvaz. It should be noted that these values were displayed automatically with 95% confidence intervals due to the availability of available epidemiological documents.

3. Results

The relationship between lung cancer and particulate matter smaller than 2.5 was analyzed using AirQ+ modeling software in Ahvaz (2008-2017). The average annual concentration of PM_{2.5} pollutants in the study period is shown in Figure 1. The highest concentration of PM_{2.5} was observed in 2010 (70.72 μ g /m³) and the lowest concentration in 2014 (41.97 μ g /m³) in Ahvaz. As can be seen from Figure 1, in all years of measurement, the amount of PM_{2.5} pollutants in the air of Ahvaz was higher than the standard set (10 g/m³) by WHO [22]. Some researchers have reported higher concentrations of PM_{2.5} than standard air pollution in other cities worldwide [11, 23]. Ahvaz is one of the most polluted cities globally regarding PM_{2.5} particulate matter. Therefore, among the pollutants of PM_{2.5} for the air of Ahvaz city, we can mention factors, such as dust storms, rapid economic growth, motor vehicles, and the existence of large industries, including large southern oil companies in the region. It is located in a dry area in southwestern Iran in the adjacency of Iraq, Saudi Arabia, and Kuwait, the main sources of dust events in the Middle East [24, 25].

The results of Table 1 show the relative risk of $PM_{2.5}$ contamination in death due to lung cancer in adults over 30 years of age between 2008 and 2017 in Ahvaz. In this case, the highest rate was 585185 people, and the base-line incidence rate was 15.55 in 2017. The highest and lowest relative risk of lung cancer deaths was 1.63 and 1.11 in 2010 and 1.06 and 1.42 in 2014, respectively.

Comparison of the percentage of attributable component of Table 2 related to $PM_{2.5}$ pollutant in death due to lung cancer in adults over 30 years of age from 2008 to 2017 in Ahvaz showed that the highest and lowest percentages of attributable component, respectively were 9.91 and 38.92] in 2010 and 5.66 and 30.06 in 2014.

Comparison of the number of attributable cases to 100,000 people at risk of Table 3 related to PM_{2.5} in death due to lung cancer in adults over 30 years of age from 2008 to 2017 in Ahvaz showed that the highest and lowest rates were 1.54 and 6.05 in 2010 and 0.88 and 4.67 in 2014, respectively.



Figure 1. Average annual concentration of PM25 pollutant during 2008-2017 in Ahvaz





Table 1. Comparison of the relative risk attributable to PM2.5 in death due to lung cancer in adults (+30 years; Ahvaz city, 2008-2017)

Year of Study	Average Annual Concentration	People at Risk	Incidence [100 thousand people]	Relative Risk (average)	Highest	Lowest
2008	50.17	545640	15.55	1.30	1.49	1.08
2009	39.65	550460	15.55	1.37	1.60	1.10
2010	70.73	544340	15.55	1.40	1.63	1.11
2011	51.44	560034	15.55	1.30	1.50	1.08
2012	57.30	564446	15.55	1.33	1.54	1.09
2013	48.77	570857	15.55	1.29	1.48	1.07
2014	41.98	574731	15.55	1.25	1.42	1.06
2015	47.39	578295	15.55	1.28	1.47	1.07
2017	47.87	581881	15.55	1.28	1.47	1.07
2017	47.97	585185	15.55	1.28	1.47	1.07

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Comparison of all Table 4 attributable cases related to $PM_{2.5}$ in death due to lung cancer in adults over 30 years of age during the years 2008 to 2017 in Ahvaz showed that the highest and lowest rates were 8 and 33 people in 2010 and 5 and 27 people in 2014, respectively.

4. Discussion

The highest and lowest concentrations of $PM_{2.5}$ pollutants were 70.72 and 41.97 μ g /m³ in 2010 and 2014,

respectively, and in all the studied years, the amount of $PM_{2.5}$ was higher than the WHO standard (10 µg /m³), which indicates the air pollution of this city in terms of this pollutant. During the ten years studied, the highest proportions and attributable cases of AP, BE, and NE were observed in all health outcomes in 2010, associated with the highest concentration of $PM_{2.5}$. It can be said that there was a significant relationship between $PM_{2.5}$ concentration, proportion, and attributable cases in all health outcomes. Thus, with increasing $PM_{2.5}$

Table 2. Comparison of PM2.5 attributable component in death due to lung cancer in adults (+30 years; Ahvaz city, 2008-2017)

Year of Study	Average Annual Concentration	People at Risk	Incidence [100 thousand people]	Attributable Component (%)	Highest	Lowest
2008	50.17	545640	15.55	23.08	32.97	7.41
2009	39.65	550460	15.55	27.21	37.5	9.09
2010	70.73	544340	15.55	28.57	38.92	9.91
2011	51.44	560034	15.55	23.34	33.53	7.41
2012	57.30	564446	15.55	24.99	35.19	8.26
2013	48.77	570857	15.55	22.48	32.43	6.54
2014	41.98	574731	15.55	20.63	30.06	5.66
2015	47.39	578295	15.55	22.12	32.16	6.54
2017	47.87	581881	15.55	22.41	32.38	6.54
2017	47.97	585185	15.55	22.47	32.42	6.54





Table 3. Comparison of the number of attributable cases of 100,000 people to $PM_{2.5}$ in death due to lung cancer in adults (+30 years; Ahvaz city, 2008-2017)

Year of Study	Average Annual Concentration	People at Risk	Incidence [100 thousand people]	The Number of Attributable Cases to 100,000 People at Risk	Highest	Lowest
2008	50.17	545640	15.55	3.59	5.13	1.15
2009	39.65	550460	15.55	4.23	5.83	1.41
2010	70.73	544340	15.55	4.44	6.05	1.54
2011	51.44	560034	15.55	3.63	5.21	1.15
2012	57.30	564446	15.55	3.89	5.41	1.09
2013	48.77	570857	15.55	3.50	5.04	1.02
2014	41.98	574731	15.55	3.21	4.67	0.88
2015	47.39	578295	15.55	3.44	5	1.02
2017	47.87	581881	15.55	3.48	5.03	1.02
2017	47.97	585185	15.55	3.49	5.04	1.02

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concentration, mortality and risk of these diseases increased. These results have been shown in some similar studies. For example, the main reason for a decline in mortality due to all causes in this study was mainly a decrease in baseline mortalities [21]. Regarding the deaths due to lung cancer, one of the deadliest types of cancer, the highest rate was 28.57% (2010) and the lowest was (20.63% 2014). The highest and lowest attributable individuals were observed in 100,000 individuals: 4 (2010) and 3 (2014), respectively. Also, the highest and lowest total attributable individuals

Table 4. Comparison of the total number of attributable cases to PM_{25} in death due to lung cancer in adults (+30 years; Ahvaz city, 2008-2017)

Year of Study	Average An- nual Concen- tration	People at Risk	Incidence [100 thousand people]	Total Number of Attributable Cases	Highest	Lowest
2008	50.17	545640	15.55	20	28	6
2009	39.65	550460	15.55	23	32	8
2010	70.73	544340	15.55	24	33	8
2011	51.44	560034	15.55	20	29	6
2012	57.30	564446	15.55	22	31	7
2013	48.77	570857	15.55	20	32	6
2014	41.98	574731	15.55	18	27	5
2015	47.39	578295	15.55	20	29	6
2017	47.87	581881	15.55	20	29	6
2017	47.97	585185	15.55	20	30	6





were 24 (2010) and 18 (2014), respectively. This outcome was evaluated in adults over 30 years of age, and the results showed that with increasing $PM_{2.5}$ concentration, the attributable cases also increased. There was a significant relationship between $PM_{2.5}$ concentration, proportion, and attributes.

In 2010, with the highest proportion and attributable cases in the population of 544,340 adults over 30 years, had the highest amount of PM25 air pollution with a concentration of 72.70 µg /m3. Therefore, appropriate measures and policies should be determined to reduce the concentration of PM25 pollutants in the air of Ahvaz to reduce the health impacts on the residents of this city. PM₂₅ particles remain in the air longer (days or weeks) and for longer distances than larger PM₁₀ particles, which are formed by smoke from factories, agriculture, and roads, as well as plant pollen, molds, and spores. However, the results of the comprehensive document seeking protection from air pollution and reducing its health outcomes show that due to the impacts of longterm exposure to particulate matter (PM_{2.5}), in 2015, an average of 11,888 people died in ten selected cities of the country with a population of more than 20 million people. The results showed that in 2015, an average of 5834 people lost their lives in Tehran due to prolonged exposure to particulate matter (PM2.5) [22, 23].

The average annual concentration of particulate matter was 31.87 μ g/m³. Also, of these deaths in the capital, an average of 129 were due to lung cancer attributable to long-term exposure to particulate matter (PM_{2.5}). According to the document, in ten selected cities of Iran, the average concentration of particulate matter (PM_{γ_s}) in 2015 was 3.2 times the national standard and the WHO guideline, which shows a large gap between the average annual concentration of particulate matter $(PM_{2,s})$ with the WHO guidance [24, 25]. Also, according to these statistics, in the city of Ahvaz, with an average annual concentration of $60.80 \,\mu g/m^3$ (twice the capital), the mortality rate was 1339 people; in other words, 22% of the capital [26, 27]. Also, mortality in Mashhad with an average annual concentration of 30.06 µg/m³, Isfahan with an average of 37.3 μ g, Tabriz with an average of 22.7 µg, Shiraz with an average of 26.8 µg, Arak with an average of 23.6 µg, Khorram Abad with an average of 23.9 µg, Sanandaj with an average of 25 µg, and Ilam with an average of 28.1 µg, were equal to 1382 people, 1471, 533, 692, 207, 211, 140, and 79 people, respectively [28]. Accordingly, it has been shown that air pollution can reduce the burden of stroke, heart disease, lung cancer, and acute and chronic respiratory diseases, and according to studies, a decrease of 10 m3 in the concentration of fine particulate matter ($PM_{2.5}$) increases life expectancy by about 0.61 years [29]. The present study results showed that appropriate measures and policies should be adopted to reduce air pollution in the control of $PM_{2.5}$ sources of pollution to reduce the health impacts of this pollutant in urban residents.

4. Conclusion

In general, the present study results showed that with increasing the concentration of PM25, the relative risk, percentage of attributable component, and attributable cases increases, respectively. Dastoorpour et al. (2019) showed a significant increase in hospitalization for respiratory patients and lung cancer attributable to SO₂ in Ahvaz. Another study found that long-term exposure to PM₂₅ and PM10 pollutants was associated with increased IHD-induced death and stroke risk among California public school female teachers [30]. In a study on the long-term trend and health impact of PM₂₅ and O3 in Tehran (2006-2015), the mortality rate for all causes for NE decreased from 5300 in 2006 (first year) to 3775 in 2015 (the tenth year). The results showed that $PM_{2,c}$ pollutants could be effective in people with lung cancer. In a study conducted in Taiwan on air pollution and lung cancer in non-smokers by examining changes in the prevalence of smoking, PM, and PM25 particulate matter, it was found that more than 50% of patients with lung cancer had never smoked, and changes in PM₂, concentration can affect the incidence and survival of this disease [31].

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the Islamic Azad University of Ahvaz (Code: 1064823910064381396183257).

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Authors' contributions

Conceptualization and supervision: All authors; Methodology: Elahe Zallaghi; Investigation: Sima Sabzalipour; Writing: Elahe Zallaghi; Original Draft: Gholamreza Goodarzi; Writing - review and editing: Alireza Zarasvandi; Data collection: All authors; Data analysis, acquisition and resources: All authors.



Conflict of interest

The authors declared no conflicts of interests regarding the publication of this manuscript. Furthermore, the authors have completely observed the ethical issues, including plagiarism, informed consent, misconduct, data fabrication and falsification, double publication and submission, and redundancy.

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