Environmental Science and Pollution Research
https://doi.org/10.1007/s11356-021-14148-2

REVIEW ARTICLE

Blood lead level monitoring related to environmental exposure in the general Iranian population: a systematic review and meta-analysis

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Received: 15 February 2021 / Accepted: 22 April 2021

Abstract

Exposure to lead can cause adverse health problems incorporating hypophosphatemia, heart and liver disease, cancers, neurological and cardiovascular diseases, central nervous disorders, and sensory disorders. This study investigated the blood lead level in the general Iranian population with environmental exposure to lead. In the presented systematic review and meta-analysis, the authors searched Iranian dataset, including Magiran, SID, Iranmedex, and Nopa, and the main dataset, comprising PubMed, Scopus, Embase, and Web of Science, all available articles until 12 January 2019, and extracting 55 studies (with 63 data for analysis) to a meta-analysis. A comprehensive meta-analysis software, pooled standard deviation, mean, sample size, and the utterly random effects model was analyzed in this study. The results showed that the overall mean BLL (95% CI) in total inquiries was 6.41 μg/dL (5.96 to 6.87). Besides, the results for gender and age subgroups were as follows: mean BLL, 6.47 μg/dL, 95% CI, 5.79, to 7.15, mean BLL, 6.44 μg/dL, 95% CI, 5.96, to 6.91, respectively. Conclusively the mean BLL in the Iranian population was higher than the recommended level by the US Centers for Disease Control and Prevention (CDC). Results indicated that the mean BLL in men and adults was more elevated than in women and children, respectively. Therefore, BLL monitoring and screening of the general Iranian population are is necessary to determine a reference value.

Keywords Blood lead levels · Lead · Pb · Exposure · Meta-analysis · Iran

Introduction

Heavy metal toxicity is considered an environmental concern because of their bioaccumulation and non-biodegradability in nature (Gautam et al. 2015). Lead (Pb) is a severely toxic and widely used heavy metal globally, which has an adverse health effect on humans and the environment (World Health Organization 2011). The lead element's properties include being odorless, silver-white in color, smooth, highly flexible, directorial, and a poor conductor of electricity, making it suitable for use in most industrial activities. Smelting of ores, mining, burning of coal, effluents from storage battery industries, automobile exhausts, metal plating, leather tanning, fertilizers, and pesticides, as well as additives in pigments and gasoline, are usually anthropogenic sources of lead pollution in the environment (Kushwaha et al. 2018). Despite the lead dangers, it is still widely used in various industries due to its desirable physical properties. Furthermore, lead was released into the environment because of the old products' recycling process worldwide (Hashemi et al. 2020).

However, most people in the world are inevitably exposed to toxic and chemical elements by increasing anthropogenic resources (Yedomon et al. 2017). In adults, chronic exposure to heavy metals such as arsenic and lead is an established risk factor for hypophosphatemia, heart and liver disease, cancers, and neurological and cardiovascular diseases (Skoczyńska et al. 2007; Hasanvand et al. 2020), as well as central nervous

Responsible Editor: Lotfi Aleya

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and intellectual disorders (Lanphear et al. 2005), sensory disorders (Cai et al. 2019), and hypertension (Martin et al. 2006). Besides, pregnant women with more blood lead levels (BLL) are at risk of miscarriage. Lead causes neurobehavioral damage, hyperactivity, hearing impairment in children, and delayed puberty in girls even at the lowest blood concentrations (Tsoi et al. 2016). Generally accumulated lead can cause various cardiovascular system problems, kidneys, bones, brain, gastrointestinal tract, and liver. Lead may cause serious health problems, including acute and chronic lead poisoning, pathological changes at multiple organs, anemia, neuropathy, and nephropathy, even in high accumulation leads to cancer. It can also be indicated that lead can cross the placenta and being detected in the fetal brain (Rostami et al. 2021).

According to the World Health Organization (WHO), there is no safe level of exposure to lead (Landrigan et al. 2018). Based on results published by the NHANES from 2007 to 2010, the reference value for blood lead was determined 5 μg/dL (Caldwell et al. 2017). Also, studies remark that if the blood lead levels reach 10 or even less than 5 μg/dL, there is still a risk of severe and neurobehavioral disorders. When employees are exposed to various pollution types in their working environment, this exposure does not exceed the threshold. Nevertheless, exposure to low levels of pollutants along the time can lead to detrimental health effects considered environmental exposure. On the other hand, legal and applicable restrictions for the pollutant concentrations present in employees' workplaces are defined as the occupational exposure standard (Nouioui et al. 2019). Usually, the amount of lead that enters the body can be excreted in urine and bile at a rate of 1 to 3 ml per minute with a half-life time of nearly 30 days.

The remaining lead is distributed through red blood cells in the smooth tissues and the final residue stored in the hard tissues such as bones. The bones' stored lead re-enters the bloodstream due to processes such as menopause, pregnancy, and lactation (Mason 2014). The highest disease burden from lead was in underdeveloped or developing countries. Base on the declaration Institute for Health Metrics and Evaluation (IHME), 1.06 million death and 24.4 million years of healthy life lost (disability-adjusted life years (DALYs)) worldwide due to lead exposure long-term accounted for in 2017.

Research of the IHME also assesses that in 2016, lead exposure was considered for 63. 2% of the global burden of idiopathic developmental and intellectual disability, 10.3% of the global burden of hypertensive heart disease, 5.6% of the world burden of the ischemic, and 6.2% of the world burden of stroke (WHO 2019). The major environmental sources of lead exposure and intake including air, dust, food and beverage, smoking, grains, and fruits produced with contaminated water or in contaminated soil pottery and crystal (Yaman 1999). However, biomonitoring of biological matrices is a useful technique to evaluate exposure to environmental and occupational trace elements and their effects (Haines et al. 2017). Biomarkers measured in blood, urine, hair, or other tissues are extensively used as indicators of exposure in the general population (Angerer et al. 2007). Different used matrices for biomonitoring are dependent on the type of material, the amount of media demanded experiment, and the limit of detection for the chemical assay. Among the various matrices, blood is a desirable choice for biological monitoring despite the difficulties in sampling. Blood is in balance with the organs and tissues in which chemicals are stored by circulating in all body (Esteban and Castaño 2009). Furthermore, the blood matrix reflects both recent and ongoing exposure to lead and bone lead levels (Brito et al. 2005). Global burden disease (GBD) study estimates the portion of DALY's environmental risk factors with nine environmental risk factors, including lead exposure, and rankings countries accordingly. In Iran, lead exposure had increased from 14.0% in 1990 to 19.4% in 2017. According to GBD results, the portion of environmental risk factors in the total disease burden in Iran)1990 (in terms of DALY index and the number of deaths was about 7 and 11 percent that increased to 8 and 13 in 2017, respectively. In 2017, based on the DALY rate index of the burden of the attributed disease to lead exposure, the value of this index in Iran was slightly higher than the regional level (3.41 vs 4.37). The local rank was 22, considering the DALY coefficient and increased mortality and exposure to lead at a low regional level (Naddafi et al. 2019). There is no large-scale national or provincial monitoring program for chemical compounds and heavy metals in Iran. Just few studies are available for occupational exposure to specific metal and trace elements in the blood or lead and specific disease relations. Therefore, this study aimed to analyze the blood lead levels in Iranian people with natural exposure and investigate the lead sources in the blood. It is hoped that this study's results increased the needs of determining specific reference value for people and encouraged the country's policymakers to demonstrate federal laws for lead exposure reduction.

Methods

Search strategy

In the template setting for this meta-analysis, first, we searched Iranian database, including Magiran, SID, Iranmedex, and Nopa, and the main database comprising PubMed, Scopus, Embase, and Web of Science, intending to find studies about BLL in the general Iranian population with environmental exposure. For this purpose, we defined a search strategy by the keywords of ((lead), (Heavy metal), (Pb), (blood), and (Iranpour et al.)) in mesh and appropriated text words by each mentioned database. The search was conducted for all articles until 2019 and updated by 2020. To find possible missing papers, the electronic domestic base data were manually searched.

Inclusion and exclusion criteria

Inclusion and exclusion designed criteria for the studied articles were as follows:

(1) Papers contain the BLL in the human population of Iran, (2) the matrix evaluated was only blood, (3) the whole searched articles were until 2020, (4) the reviewed articles' languages were English and Farsi, and (5) the abstracts, books, presentations, meta-analysis, reviews, and letters to the editor were excluded from the study.

Firstly, duplicate articles were removed to decrease the authors' workload, and the remaining relevant papers were reviewed by the title and the keyword and abstracts by the reviewers (N.KH. and N.A.). The articles were screened as follows: (1) the study should contain statistical mean and standard deviation (S.D.) or standard error (S.E.) for BLL in the original dataset; (2) studies reporting lead levels in other media such as hair, serum, milk, bone, and urine are excluded; (3) studies reporting lead levels in the workplace, occupational, and poisoning were also excluded because they were subjected to occupational exposure as mentioned above; (4) in this research, the studies' design was also considered as exclusion criteria. Generally, the reviewed articles consisted of two groups, either articles that directly measured BLL in people with environmental exposure or compared BLL in cases (patient, addict, or occupational exposure) and controls (healthy individuals), but in this paper, only BLL in the control groups were included, and the cases were ignored because they were not representative for environmental exposure. After screening the articles by the title and abstract, some articles' acceptance or rejection is tricky; therefore, the items' full text was downloaded. Besides, any disagreement between the two reviewers was discussed by the supervisor. Finally, in the screened articles, the following information was essential and extracted: the author's name, location of study, study design, title and year of study, a matrix containing lead, sample size, mean, and the S.D. (or S.E.) of BLL, age, and gender.

Meta-analysis of data

Data extracted from screened articles containing arithmetic mean, the S.D. of BLL, and sample size were quantitatively analyzed. Commonly, meta-analyses performed use random effects (R.E.) or fixed effects (F.E.) model. Fixed effects models consider the variation only and do not presume differences between studies. If the effect size has real value for all research and any variation occurs due to sampling error, the F.E. model is appropriate (Borenstein et al. 2010). On the other hand, random effects models assume that studies display a random sampling of different populations within a more "super" population (Dersimonian and Kacker 2007). So the observed variance in an R.E. model in the reviewed studies is assumed to be partially real between the sampled groups (Borenstein et al. 2010). This study assumed that the samples display the variance based on the population to some extent, so a random effect model according to sample size, the mean. and standard deviation of BLL, was pooled using comprehensive meta-analysis software (CMA; version 2.2.064). Researchers usually prove heterogeneity of studies by I^2 statistics, which is generally expressed in three levels of 0.25, 0.50, and 0.75, indicating low, medium, and high heterogeneity. Furthermore, the *P*-value of Q-statistics (less than 0.10) is another factor in determining heterogeneity.

The significant heterogeneity represents the portion of the total variance in the observed effects due to random variance (Higgins et al. 2003; Vlasak et al. 2019). To assess the heterogeneity, subgroup analysis, including age and gender, was applied.

Results

Systematic review

Description of studies of BLL during time

As shown in Fig. 2, the average BLL measured from 1983 to 2019 in review articles decreased from 22 μg/dL to 5.59 μg/dL.

PRISMA flow diagram represents the process of entering studies into this meta-analysis. By searching the sites, including Web of Science, Scopus, Embase, and PubMed, we obtained 1498, 805, 400, and 228 original English papers, respectively. Also, the domestic search included 195 articles from the internal sites, generally, 3707 articles in all databases, in which 1370 duplicate articles were removed. Finally, 113 papers had included our criteria for furthermore analysis. After downloading the full text and screening, 49 documents meet our criteria (mean and standard deviation of BLL and sample size); also 6 articles were manually added to the analysis. Because some studies measured BLL in two or more groups of the population, finally, 55 studies in quantitative synthesis (meta-analysis) were entered, which contains 63 data rows (including mean and standard deviation of BLL and sample size).

Description of studies of BLL in location

Figure 3 shows the mean BLL of reviewed studies by the city or area where the research was conducted. The highest and lowest average BLL is 13.21 μg/dL and 0.65 μg/dL, respectively.

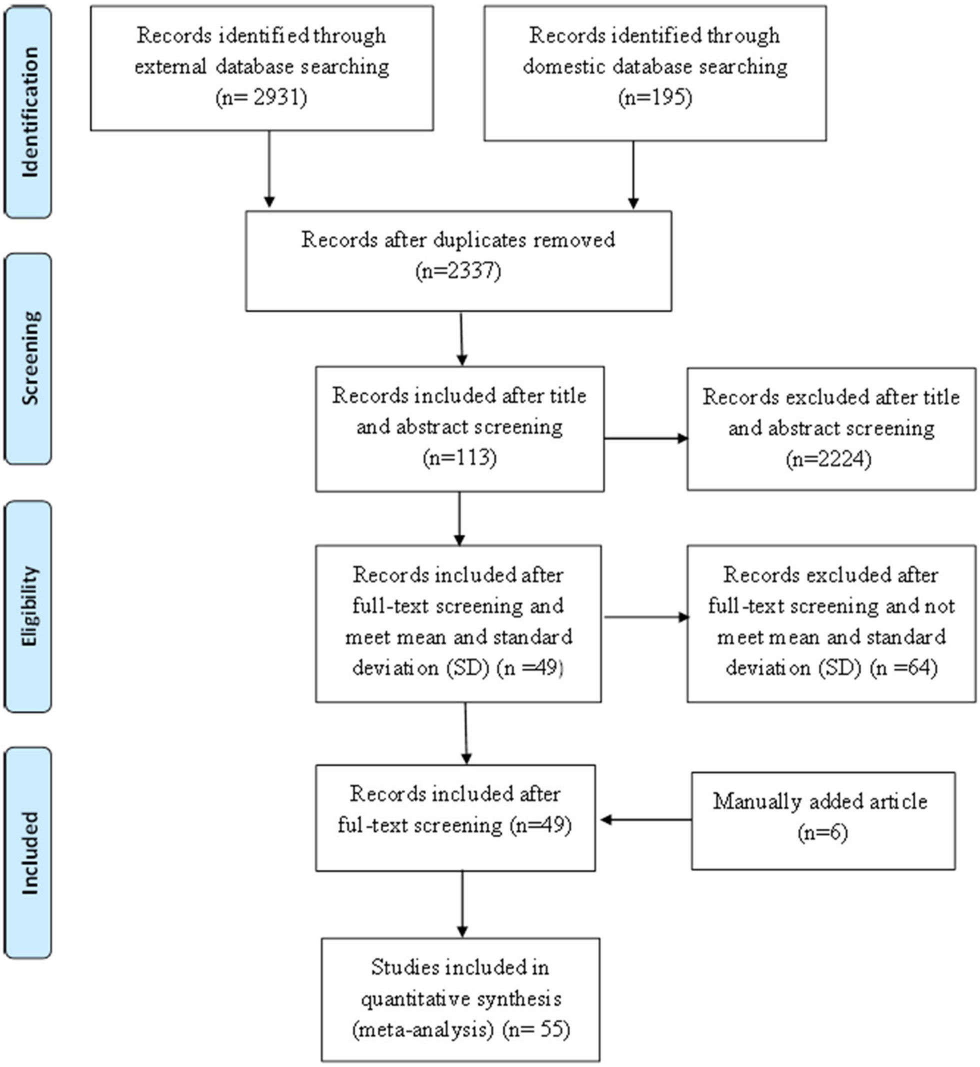


Fig. 1 PRISMA flow diagram

Characteristics of studies included in the meta-analysis

The statistical population of studies that entered the meta-analysis included men, women, and children separately and papers that did not segregate the sexes or examined both sexes with a total sample size of 9132 (Table 1). The data were

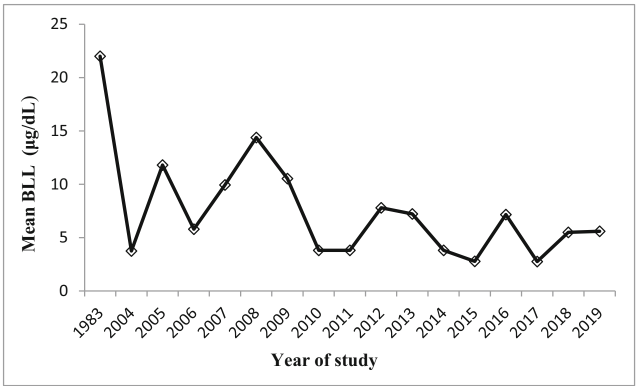


Fig. 2 Description of studies of BLL during time

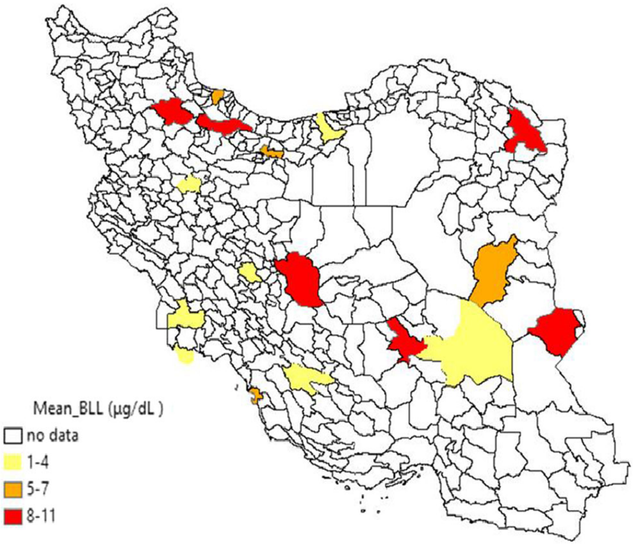


Fig. 3 Description of studies of BLL in location

Table 1 Details of studies included in the meta-analysis

Study No.	Location	Year of study	BLL (μg/dL)		Sample Size	Subgroups	References
			Mean	± SD			
1	Tehran	1980–1981	22	10.00	830	Men and women	(Ghafourian et al. 1983)
2	Tehran	2001	4.8	1.9	55	Women	(Vigeh et al. 2004)
3	Tehran	2002	2.7	0.3	80	Men and women	(Dizaji et al. 2004)
4	Mashad	2001–2003	11.80	3.21	111	Child	(Farhat et al. 2005)
5	Tehran	2002–2003	2.6	0.3	80	Men	(Bakhtiarian et al. 2006)
6	Tehran	2003–2004	4.82	2.22	396	Women	(Vigeh et al. 2006)
7	Tehran	2003–2004	3.52	2.09	396	Child	(Vigeh et al. 2006)
8	Mashad	2001–2002	12.19	3.35	206	Child	(Farhat et al. 2006)
9	Isfahan	2005	11.30	1.90	34	Child	(Iranpour et al. 2007)
10	Isfahan	2005	13.52	2.69	34	Women	(Iranpour et al. 2007)
11	Zanjan	2005	15.57	13.35	36	Child	(Mahram et al. 2007)
12	Rasht	2005	7.6	4.1	86	Women	(Golmohammadi et al. 2007)
13	Rasht	2005	5.9	3.2	86	Child	(Golmohammadi et al. 2007)
14	Tehran	2005	9.1	8.4	85	Women	(Golmohammadi et al. 2007)
15	Tehran	2005	6.6	5.2	85	Child	(Golmohammadi et al. 2007)
16	Mashad	2006	16.38	5.71	16	Child	(Deldar et al. 2008)
17	Tehran	2006	12.37	5.64	101	Men and women	(Farzin et al. 2008)
18	Rafsanjan	2008	8.6	3.5	22	Men	(Salehi et al. 2009)
19	Mashad	2005	12.46	17.5	40	Women	(Mansoori et al. 2009)
20	Tehran	2006	3.8	2	15	Women	(Vigeh et al. 2010)
21	Tehran	2006	3.8	2	348	Women	(Vigeh et al. 2011)
22	Tehran	2010	16.7	12.51	39	Men	(Amiri and Amini 2012)
23	Tehran	2010–2011	4.7	4.9	1033	Women	(Behjat et al. 2012)
24	Tehran	2007–2010	7.18	3.18	100	Child	(Sepideh et al. 2012)
25	Tehran	2011	2.73	0.94	75	Women	(Chehrazi and Banaem 2012)
26	Tehran	2011	2.83	1.31	75	Child	(Vida Nezhad and Lida Moghadam, 2012)
27	Tehran	2011	12.6	2.3	51	Women	(Sadeghi et al. 2012)
28	Tehran	2010–2011	14.52	4.61	100	Men and women	(Farzin et al. 2013)
29	Tehran	2009	9.33	18.42	62	Men	(Sadeghniiat-Haghighi et al. 2013)
30	Sari	2010–2011	3.35	1.64	165	Child	(Ghaffari et al. 2013)
31	Ahvaz	2011	1.67	0.68	33	Men and women	(Jalali et al. 2013)
32	Tehran	2009–2010	6.05	1.83	48	Men	(Domeneh et al. 2014)
33	Tehran	2012	2.97	2.24	60	Child	(Khosravi et al. 2014)
34	Tehran	2010–2011	4.7	4.9	110	Women	(Leila et al. 2014)
35	Tehran	2013	4.7	4.9	1033	Women	(Alian et al. 2014)
36	iran	2013	0.65	0.15	160	Men and women	(Poursafa et al. 2014)
37	Tehran	2012–2013	2.78	2.77	30	Child	(Afshar et al. 2015)
38	Tehran	2013–2014	5.71	3.37	74	Men	(Aliomrani et al. 2016)
39	Zabol	2015	9.86	4.4	78	Men	(Nemati et al. 2016)
40	Qazvin	2014	10.01	5.82	30	Men	(Mehrtash et al. 2016)
41	Zanjan	2015–2016	6.24	1.74	79	Women	(Bayat et al. 2016)
42	Mashhad	2015	5.42	1.46	40	Men	(Khatibi-Moghadam et al. 2016)
43	Birjand	2016	5.73	2.74	33	Men and women	(Mehrpour et al. 2016)
44	Hamadan	2016	4.02	3.16	40	Men	(Afzali et al. 2017)

Table 1 (continued)

Study No.	Location	Year of study	BLL (μg/dL)		Sample Size	Subgroups	References
			Mean	± SD			
45	Birjand	2014	5.73	4.77	33	Men	(Ghaemi et al. 2017)
46	Abadan	2013	0.65	0.32	147	Child	(Neda et al. 2017)
47	Shahrekord	2013	0.69	0.79	262	Child	(Panahandeh et al. 2017)
48	Shiraz	2013–2014	2.71	2.29	68	Child	(Parhoudeh et al. 2018)
49	Birjand	2016–2017	7.88	6.63	54	Men and women	(Fathabadi et al. 2018)
50	Khorasan	2017	5.11	7.41	400	Men and women	(Khorashadizadeh et al. 2018)
51	Zanjan	2015	7.34	4.29	150	Child	(Marzban et al. 2018)
52	Ahvaz	2017	1.672	0.684	33	Men and women	(Shahbazian et al. 2018)
53	Tehran	2016–2017	9.79	4.31	150	Women	(Dalili et al. 2019)
54	Tehran	2016–2017	8.29	4.83	150	Child	(Dalili et al. 2019)
55	Birjand	2017	3.38	2.88	29	Men and women	(Dehghanifiroozabadi et al. 2019)
56	Tehran	2017–2018	8.58	3.4	40	Men	(Fakoor et al. 2019)
57	Bushehr	2012	4.69	4.08	148	Child	(Gizo et al. 2019)
58	Bushehr	2012	4.85	4.31	124	Child	(Gizo et al. 2019)
59	Kerman	2016	3.58	6.09	31	Men	(Ahmadinejad et al. 2019b)
60	Isfahan	2017	3.01	0.1	63	Women	(Movahedi et al. 2019)
61	Birjand	2017	6.02	7.41	400	Men and women	(Nakhaee et al. 2019)
62	Shiraz	2017–2018	2.95	0.7	60	Women	(Rezaie et al. 2019)
63	Mashhad	2014–2015	6.37	5.93	100	Child	(Torabian et al. 2019)

classified into age and gender subgroups, including 21, 13, and 17 articles for children, men, and women, respectively. Furthermore, 12 articles measured BLL in both sexes (men and women). Finally, the effect of gender and age was examined in this meta-analysis.

Results of meta-analysis

Figure 4 explains the forest plot summarizing the mean, standard error, and 95% confidence interval (Bjermo et al.). Due to a significant heterogeneity between studies (Q-statistic *P*-value < 0.001, I^2 = 99.84%), a random effects model was employed for data analysis. Based on the 63 studies' meta-analysis, BLL and 95% CI's mean and standard error were 6.41 μg/dL, 0.23, and 5.96 to 6.87, respectively.

Subgroup analysis

Effect of gender As mentioned above, based on gender, subgroup analysis was performed, and the results were shown in Fig. 5. As can be seen, the results illustrated mean 6.85 μg/dL, standard error 0.54, and 95% CI 5.77 to 9.92 for men; and mean 6.22 μg/dL, standard error 0.45, and 95% CI 5.34 to 7.10 for women; and mean 6.47 μg/dL, standard error 0.34, and 95% CI 5.79 to 7.15 in overall.

Effect of age A subgroup analysis was performed based on comparing BLL in adults and children, results shown in Fig. 6. Base on the analysis, the results indicated mean 6.11 μg/dL, standard error 0.41, and 95% CI 5.29 to 6.93 for children; mean 6.60 μg/dL, standard error 0.22, and 95% CI 6.02 to 7.19 in adult; and mean 6.44 μg/dL, standard error 0.24 and 95% CI 5.96 to 6.91 in overall.

Discussion

Nowadays, lead exposure is a significant cause of disease burden. The IHME stated that lead exposure's long-term health effects were responsible for the 1.06 million deaths and 24.4 million DALY in 2017(WHO 2019). Recent studies show that BLL lower than 5 μg/dL causes physical and psychological health problems. According to the CDC report, BLLs of 5 μg/dL related to decreased renal action and BLLs of 10 μg/dL correlated with increased blood pressure and hypertension. The CDC also announces that BLLs of 10 μg/dL related to a decline in I.Q. efficiency and other

Study name	Subgroup within study	Mean	Standard error	Lower limit	Upper limit	Relative weight
Ghafourian, H (1983)	Men & Women	22.000	0.347	21.320	22.680	1.69
Vigeh, M. (2004)	Women	4.800	0.256	4.298	5.302	1.72
Dizaji, R (2004)	Men & Women	2.700	0.034	2.634	2.766	1.76
Farhat, A (2005)	Child	11.803	0.305	11.206	12.400	1.71
Bakhtiarian, A (2006)	Men	2.600	0.034	2.534	2.666	1.76
Vigeh, M. 1 (2006)	Women	4.820	0.112	4.601	5.039	1.75
Vigeh, M. 2 (2006)	Child	3.520	0.105	3.314	3.726	1.75
Farhat.Sh (2006)	Child	12.195	0.234	11.736	12.654	1.73
Iranpour, R. 1 (2007)	Child	11.308	0.327	10.667	11.949	1.70
Iranpour, R. 2 (2007)	Women	13.526	0.462	12.621	14.431	1.64
Mahram, M (2007)	Child	15.570	2.225	11.209	19.931	0.67
Golmohamadi, T 1 (2007)	Women	7.600	0.442	6.733	8.467	1.65
Golmohamadi, T 2 (2007)	Child	5.900	0.345	5.224	6.576	1.69
Golmohamadi, T 3 (2007)	Women	9.100	0.911	7.314	10.886	1.38
Golmohamadi, T4 (2007)	Child	6.600	0.564	5.495	7.705	1.59
Deldar, K (2008)	Child	16.381	1.430	13.579	19.183	1.05
Farzin, L (2008)	Men & Women	12.375	0.561	11.275	13.475	1.59
Salehi, H (2009)	Men	8.600	0.746	7.137	10.063	1.49
Mansoori, M (2009)	Women	12.460	2.767	7.037	17.883	0.50
Vigeh, M (2010)	Women	3.800	0.516	2.788	4.812	1.62
Vigeh, M (2011)	Women	3.800	0.107	3.590	4.010	1.75
Amiri, M (2012)	Men	16.700	2.003	12.774	20.626	0.76
Afkhami, B (2012)	Women	4.700	0.152	4.401	4.999	1.75
Daroogar, S (2012)	Child	7.189	0.319	6.565	7.813	1.70
Nezhad, Chehrazi, V 1 (2012)	Women	2.730	0.109	2.517	2.943	1.75
Nezhad, Chehrazi, V2 (2012)	Child	2.830	0.151	2.534	3.126	1.75
Sadeghi, F (2012)	Women	12.600	0.322	11.969	13.231	1.70
Farzin, L. (2013)	Men & Women	14.521	0.461	13.617	15.425	1.64
Sadeghniiat-Haghighi, Kh (2013)	Men	9.330	2.339	4.745	13.915	0.63
Ghaffari,J (2013)	Child	3.350	0.128	3.100	3.600	1.75
Jalali, MT (2013)	Men & Women	1.670	0.118	1.438	1.902	1.75
Domeneh, B. H (2014)	Men	6.050	0.264	5.532	6.568	1.72
Khosravi, N (2014)	Child	2.970	0.289	2.403	3.537	1.71
Ghalekhandabi, L (2014)	Women	4.700	0.467	3.784	5.616	1.64
Alian, Moghadam, N (2014)	Women	4.700	0.152	4.401	4.999	1.75
Poursafa, P (2014)	Men & Women	0.650	0.012	0.627	0.673	1.76
Afshar, L (2015)	Child	2.780	0.506	1.789	3.771	1.62
Aliomrani, M (2016)	Men	5.710	0.392	4.942	6.478	1.67
Nemati, A (2016)	Men	9.860	0.498	8.884	10.836	1.63
Mehrtash, B (2016)	Men	10.010	1.063	7.927	12.093	1.28
Bayat, F (2016)	Women	6.240	0.196	5.856	6.624	1.74
Khatibi-Moghadam, H (2016)	Men	5.420	0.231	4.968	5.872	1.73
Mehrpour, O (2016)	Men & Women	5.730	0.477	4.795	6.665	1.64
Afzali, S (2017)	Men	4.020	0.500	3.041	4.999	1.62
Ghaemi, K (2017)	Men	5.730	0.830	4.103	7.357	1.43
Neda, A. N (2017)	Child	0.650	0.026	0.598	0.702	1.76
Panahandeh, G (2017)	Child	0.690	0.049	0.594	0.786	1.76
Parhoudeh, M (2017)	Child	2.710	0.278	2.166	3.254	1.71
Fathabadi, B (2018)	Men & Women	7.880	0.902	6.112	9.648	1.39
Khorashadizadeh, S (2018)	Men & Women	5.110	0.371	4.384	5.836	1.68
Marzban, A (2018)	Child	7.340	0.350	6.653	8.027	1.69
Shahbazian, H (2018)	Men & Women	1.672	0.119	1.439	1.905	1.75
Dalili, H 1 (2019)	Women	9.790	0.352	9.100	10.480	1.69
Dalili, H 2 (2019)	Child	8.290	0.394	7.517	9.063	1.67
Dehghanifiroozabadi, M (2019)	Men & Women	3.380	0.535	2.332	4.428	1.61
Fakoor, M (2019)	Men	8.570	0.538	7.516	9.624	1.61
Hatami, G 1 (2019)	Child	4.690	0.335	4.033	5.347	1.70
Hatami, G 2 (2019)	Child	4.850	0.387	4.091	5.609	1.68
Ahmadinejad, M (2019)	Men	3.580	1.094	1.436	5.724	1.26
Movahedi, M (2019)	Women	3.010	0.013	2.985	3.035	1.76
Nakhaee, S (2019)	Men & Women	6.020	0.371	5.294	6.746	1.68
Rezaie, M (2019)	Women	2.950	0.090	2.773	3.127	1.75
Torabian, S (2019)	Child	6.370	0.593	5.208	7.532	1.58
		6.418	0.231	5.966	6.871	

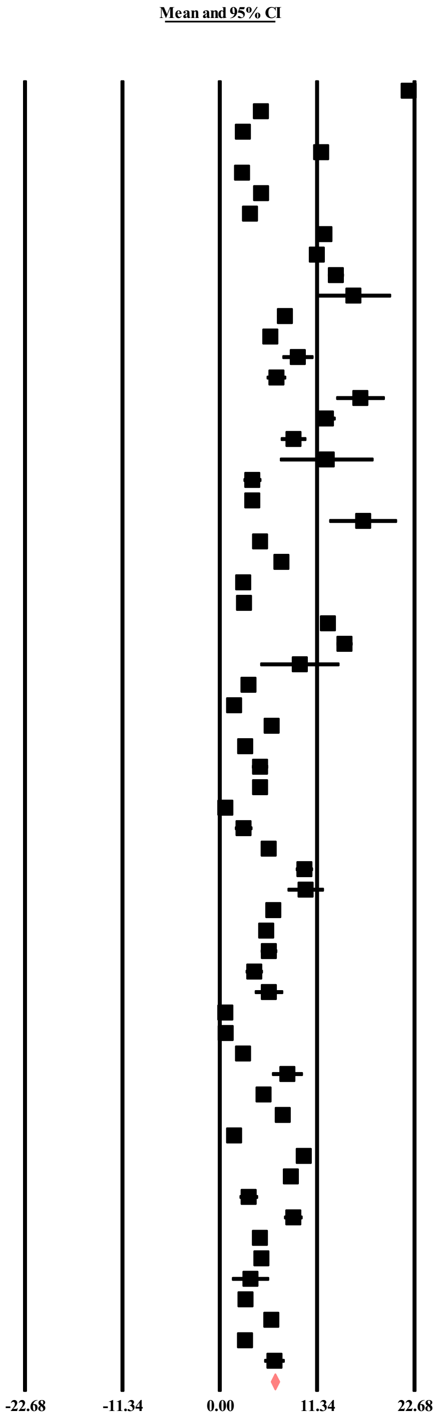
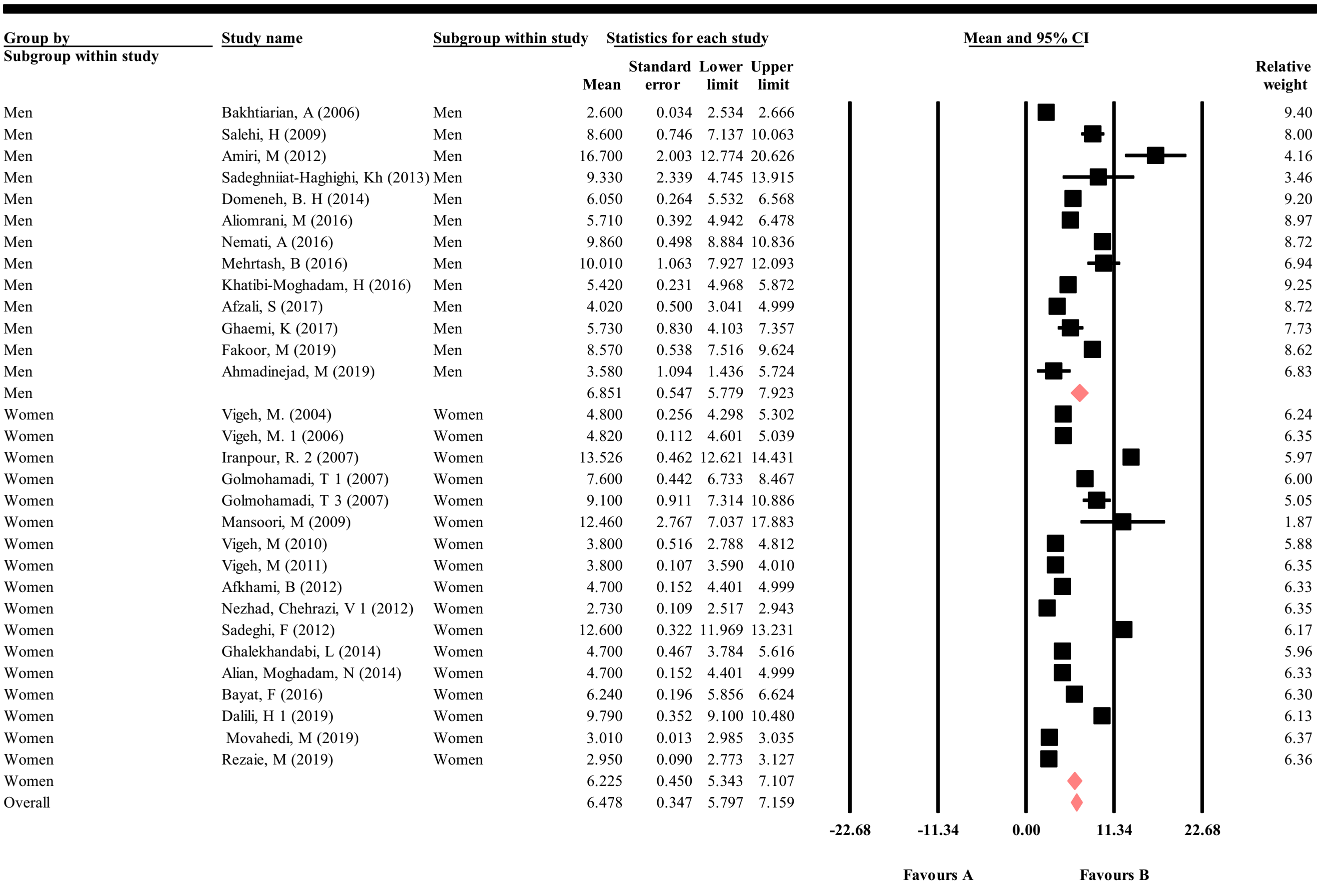


Fig. 4 Forest plots of BLL in total

neuropsychological imperfection (including decreased hearing). Also, BLLs of 15 μg/dL or more are associated with adverse effects on pregnancy (Apte et al. 2019). Lead commonly enters the human body through the respiratory and digestive systems with approximately a biological half-life of 30 days in the bloodstream. Lead in the bloodstream mainly bound to red blood cells, distributed into soft tissues, and accumulated in bones, where it can remain for 20–30 years. During these processes leading to bone matter turnover, the deposited lead is released back into circulating blood. Thus, blood levels reflect not only recent and ongoing lead exposure but also bone lead levels (Vlasak et al. 2019).

Since there is (Iranpour et al.) no national or provincial monitoring program for chemical compounds and heavy metals to set a standard for them, this meta-analysis was performed to study the status of lead in the people's blood with



Group by Subgroup within study	Study name	Subgroup within study	Statistics for each study				Relative weight
			Mean	Standard error	Lower limit	Upper limit	
Men	Bakhtiarian, A (2006)	Men	2.600	0.034	2.534	2.666	9.40
Men	Salehi, H (2009)	Men	8.600	0.746	7.137	10.063	8.00
Men	Amiri, M (2012)	Men	16.700	2.003	12.774	20.626	4.16
Men	Sadeghniiat-Haghighi, Kh (2013)	Men	9.330	2.339	4.745	13.915	3.46
Men	Domeneh, B. H (2014)	Men	6.050	0.264	5.532	6.568	9.20
Men	Aliomrani, M (2016)	Men	5.710	0.392	4.942	6.478	8.97
Men	Nemati, A (2016)	Men	9.860	0.498	8.884	10.836	8.72
Men	Mehrtash, B (2016)	Men	10.010	1.063	7.927	12.093	6.94
Men	Khatibi-Moghadam, H (2016)	Men	5.420	0.231	4.968	5.872	9.25
Men	Afzali, S (2017)	Men	4.020	0.500	3.041	4.999	8.72
Men	Ghaemi, K (2017)	Men	5.730	0.830	4.103	7.357	7.73
Men	Fakoor, M (2019)	Men	8.570	0.538	7.516	9.624	8.62
Men	Ahmadinejad, M (2019)	Men	3.580	1.094	1.436	5.724	6.83
Men			6.851	0.547	5.779	7.923	
Women	Vigeh, M. (2004)	Women	4.800	0.256	4.298	5.302	6.24
Women	Vigeh, M. 1 (2006)	Women	4.820	0.112	4.601	5.039	6.35
Women	Iranpour, R. 2 (2007)	Women	13.526	0.462	12.621	14.431	5.97
Women	Golmohamadi, T 1 (2007)	Women	7.600	0.442	6.733	8.467	6.00
Women	Golmohamadi, T 3 (2007)	Women	9.100	0.911	7.314	10.886	5.05
Women	Mansoori, M (2009)	Women	12.460	2.767	7.037	17.883	1.87
Women	Vigeh, M (2010)	Women	3.800	0.516	2.788	4.812	5.88
Women	Vigeh, M (2011)	Women	3.800	0.107	3.590	4.010	6.35
Women	Afkhami, B (2012)	Women	4.700	0.152	4.401	4.999	6.33
Women	Nezhad, Chehrazi, V 1 (2012)	Women	2.730	0.109	2.517	2.943	6.35
Women	Sadeghi, F (2012)	Women	12.600	0.322	11.969	13.231	6.17
Women	Ghalekhandabi, L (2014)	Women	4.700	0.467	3.784	5.616	5.96
Women	Alian, Moghadam, N (2014)	Women	4.700	0.152	4.401	4.999	6.33
Women	Bayat, F (2016)	Women	6.240	0.196	5.856	6.624	6.30
Women	Dalili, H 1 (2019)	Women	9.790	0.352	9.100	10.480	6.13
Women	Movahedi, M (2019)	Women	3.010	0.013	2.985	3.035	6.37
Women	Rezaie, M (2019)	Women	2.950	0.090	2.773	3.127	6.36
Women			6.225	0.450	5.343	7.107	
Overall			6.478	0.347	5.797	7.159	

Fig. 5 Forest plot comparing BLL in men and women

environmental exposure, in total and subgroups. The basis for choosing a subgroup for meta-analysis in this study was segregation in the sample size of articles (including men, women, both sexes (men and women), and child).

The age subgroup criteria were children and adults following the United Nation Convention on the Child's Rights. In this way, if the study population in the main study was 17 years or less, they were considered children. Moreover, if persons are 18 years old and older, they were considered adults (Assembly 1989). The most common methods for detecting trace metals such as lead in biological samples are high-sensitivity spectroscopic techniques such as atomic absorption spectroscopy, plasma induction coupling emission, and mass spectroscopy. Nevertheless, the method of inductively coupled plasma mass spectrometry (ICP-MS) is better and more accurate for measuring lead in the blood and plasma (Boseila et al. 2004). Tools of measurement BLL in all the articles included in this study was one of the tools mentioned above.

Therefore, due to this issue's high sensitivity, many researchers modeled the amount of lead received from different sources in the long term (Yaman 1999). In Iran until 2000, the most important lead exposure source in cities like Tehran was airborne particles. Adding lead to gasoline was legally banned in the early 2002 and is expected to reduce the amount of received lead from the air source.

Due to the phase-out of lead from consumed gasoline in Iran, the reason for increasing Iranians' blood lead levels was its use in opium to raise the weight, according to new research (Ahmadinejad et al. 2019a). Moreover, wrapping food items, including meat, sandwiches, and skinless fruits, in colored newspapers and black nylons, can raise blood lead levels. Besides, ceramic containers were the other ways of lead entering, used to store acidic substance storage. Also, cosmetic products, comprising lipsticks and hair dyes, were the other ways (Sharafi et al. 2015).

However, as Iran's capital, Tehran is a densely populated city, where despite the ban on adding lead to gasoline, it is still used. In terms of geographical location, Tehran is surrounded by mountains in three directions without any continuous air flow, making the city a polluted area (Abdollahi et al. 1995). Generally, 60–90% of lead in airborne dust of the ambient and 10– 50% of lead in the blood of the non-occupationally lead-exposed population can be attributed to lead in gasoline (Abdollahi et al. 1995). As shown in Figs. 3 and 4, the mean blood lead conducted before 2002 is higher than in recent years, 22 µg/dL and 2-8 µg/dL, respectively. In Spain, BLL dropped from 12 to 6 after a ban on adding lead to gasoline (Schuhmacher et al. 1996). In the USA, BLL measured by the

Group by Subgroup within study	Study name	Subgroup within study	Statistics for each study Mean	Standard error	Lower limit	Upper limit	Relative weight
Adult	Ghafourian, H (1983)	Adult	22.000	0.347	21.320	22.680	2.55
Adult	Vigeh, M. (2004)	Adult	4.800	0.256	4.298	5.302	2.59
Adult	Dizaji, R (2004)	Adult	2.700	0.034	2.634	2.766	2.64
Adult	Vigeh, M. 1 (2006)	Adult	4.820	0.112	4.601	5.039	2.63
Adult	Bakhtiarian, A (2006)	Adult	2.600	0.034	2.534	2.666	2.64
Adult	Iranpour, R. 2 (2007)	Adult	13.526	0.462	12.621	14.431	2.48
Adult	Golmohamadi, T 1 (2007)	Adult	7.600	0.442	6.733	8.467	2.50
Adult	Golmohamadi, T 3 (2007)	Adult	9.100	0.911	7.314	10.886	2.12
Adult	Farzin, L (2008)	Adult	12.375	0.561	11.275	13.475	2.42
Adult	Mansoori, M (2009)	Adult	12.460	2.767	7.037	17.883	0.81
Adult	Salehi, H (2009)	Adult	8.600	0.746	7.137	10.063	2.27
Adult	Vigeh, M (2010)	Adult	3.800	0.516	2.788	4.812	2.45
Adult	Vigeh, M (2011)	Adult	3.800	0.107	3.590	4.010	2.63
Adult	Afkhami, B (2012)	Adult	4.700	0.152	4.401	4.999	2.62
Adult	Nezhad, Chehrazi, V 1 (2012)	Adult	2.730	0.109	2.517	2.943	2.63
Adult	Sadeghi, F (2012)	Adult	12.600	0.322	11.969	13.231	2.56
Adult	Amiri, M (2012)	Adult	16.700	2.003	12.774	20.626	1.21
Adult	Sadeghniiat-Haghighi, Kh (2013)	Adult	9.330	2.339	4.745	13.915	1.01
Adult	Farzin, L. (2013)	Adult	14.521	0.461	13.617	15.425	2.48
Adult	Jalali, MT (2013)	Adult	1.670	0.118	1.438	1.902	2.63
Adult	Ghalekhandabi, L (2014)	Adult	4.700	0.467	3.784	5.616	2.48
Adult	Alian, Moghadam, N (2014)	Adult	4.700	0.152	4.401	4.999	2.62
Adult	Domeneh, B. H (2014)	Adult	6.050	0.264	5.532	6.568	2.59
Adult	Poursafa, P (2014)	Adult	0.650	0.012	0.627	0.673	2.64
Adult	Bayat, F (2016)	Adult	6.240	0.196	5.856	6.624	2.61
Adult	Aliomrani, M (2016)	Adult	5.710	0.392	4.942	6.478	2.53
Adult	Nemati, A (2016)	Adult	9.860	0.498	8.884	10.836	2.46
Adult	Mehrtash, B (2016)	Adult	10.010	1.063	7.927	12.093	1.98
Adult	Khatibi-Moghadam, H (2016)	Adult	5.420	0.231	4.968	5.872	2.60
Adult	Mehrpour, O (2016)	Adult	5.730	0.477	4.795	6.665	2.47
Adult	Afzali, S (2017)	Adult	4.020	0.500	3.041	4.999	2.46
Adult	Ghaemi, K (2017)	Adult	5.730	0.830	4.103	7.357	2.19
Adult	Fathabadi, B (2018)	Adult	7.880	0.902	6.112	9.648	2.13
Adult	Khorashadizadeh, S (2018)	Adult	5.110	0.371	4.384	5.836	2.54
Adult	Shahbazian, H (2018)	Adult	1.672	0.119	1.439	1.905	2.63
Adult	Dalili, H 1 (2019)	Adult	9.790	0.352	9.100	10.480	2.55
Adult	Movahedi, M (2019)	Adult	3.010	0.013	2.985	3.035	2.64
Adult	Rezaie, M (2019)	Adult	2.950	0.090	2.773	3.127	2.64
Adult	Fakoor, M (2019)	Adult	8.570	0.538	7.516	9.624	2.43
Adult	Ahmadinejad, M (2019)	Adult	3.580	1.094	1.436	5.724	1.95
Adult	Dehghanifiroozabadi, M (2019)	Adult	3.380	0.535	2.332	4.428	2.44
Adult	Nakhaee, S (2019)	Adult	6.020	0.371	5.294	6.746	2.54
Adult			6.608	0.299	6.023	7.193	
Child	Farhat, A (2005)	Child	11.803	0.305	11.206	12.400	5.01
Child	Vigeh, M. 2 (2006)	Child	3.520	0.105	3.314	3.726	5.13
Child	Farhat.Sh (2006)	Child	12.195	0.234	11.736	12.654	5.07
Child	Iranpour, R. 1 (2007)	Child	11.308	0.327	10.667	11.949	4.99
Child	Mahram, M (2007)	Child	15.570	2.225	11.209	19.931	2.09
Child	Golmohamadi, T 2 (2007)	Child	5.900	0.345	5.224	6.576	4.97
Child	Golmohamadi, T4 (2007)	Child	6.600	0.564	5.495	7.705	4.70
Child	Deldar, K (2008)	Child	16.381	1.430	13.579	19.183	3.21
Child	Daroogar, S (2012)	Child	7.189	0.319	6.565	7.813	5.00
Child	Nezhad, Chehrazi, V2 (2012)	Child	2.830	0.151	2.534	3.126	5.11
Child	Ghaffari,J (2013)	Child	3.350	0.128	3.100	3.600	5.12
Child	Khosravi, N (2014)	Child	2.970	0.289	2.403	3.537	5.02
Child	Afshar, L (2015)	Child	2.780	0.506	1.789	3.771	4.79
Child	Neda, A. N (2017)	Child	0.650	0.026	0.598	0.702	5.15
Child	Panahandeh, G (2017)	Child	0.690	0.049	0.594	0.786	5.14
Child	Parhoudeh, M (2017)	Child	2.710	0.278	2.166	3.254	5.03
Child	Marzban, A (2018)	Child	7.340	0.350	6.653	8.027	4.97
Child	Dalili, H 2 (2019)	Child	8.290	0.394	7.517	9.063	4.92
Child	Hatami, G 1 (2019)	Child	4.690	0.335	4.033	5.347	4.98
Child	Hatami, G 2 (2019)	Child	4.850	0.387	4.091	5.609	4.93
Child	Torabian, S (2019)	Child	6.370	0.593	5.208	7.532	4.66
Child			6.114	0.417	5.297	6.931	
Overall			6.440	0.243	5.965	6.916	

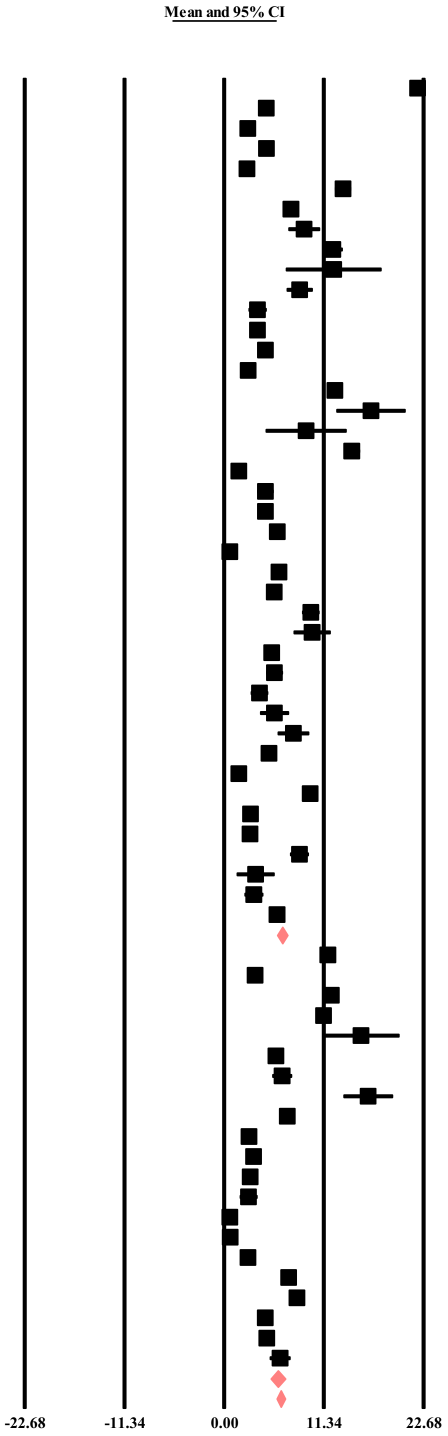


Fig. 6 Forest plot comparing BLL in child and adults

National Health and Nutrition examination survey decreased from 13.1 μg/dL to 1.64 μg/dL in 1979–1980 to 1999–2000 (Park et al. 2010). Many researchers agree that a significant factor in the lead's decline has been the phase-out of gasoline lead from 175 countries (Landrigan et al. 2018).

It should be noted that in recent studies, the role of air in lead exposure is low. Therefore, BLL is not only dependent on air pollution, but also the presence of contamination in food, water, bad health habits, lifestyle, and smoking should be considered. Even in Iran, rice grown in contaminated soil or water is another source of lead exposure.

Water resources, air, soil, some colors of ink, seafood, plants of the polluted region, etc. are considered the environmental sources for increasing lead. Based on the WHO standard and

Table 2 Random effects model, heterogeneity statistics, and model fit statistics and information criteria for total and subgroup

	Effect size and 95% CI					Test of null (2-tail)		Heterogeneity			Heterogen	Tau^2		
Scenario	Model	Estimated	Se	Lower limit	Upper limit	Z-value	P- value	Q-value	df (Q)	P-value	I^2	Tau^2	Se	Tau
Total	Random	6.41	0.23	5.96	6.87	27.80	0.00	39312.1	62	0.00	99.84	3.03	2.41	1.74
Gender	Random	6.47	0.34	5.79	7.15	18.64	0.00	0.78	1	0.37	99.22	1.43	1.40	1.19
Age	Random	6.44	0.24	5.96	6.91	26.53	0.00	0.92	1	0.33	99.84	3.03	2.41	1.74

national standard in Iran, the concentration of lead in drinking water was limited to 0.01 mg/L and 0.05 mg/L, respectively, which is higher in Iran than the WHO (Karbasi et al. 2010). Even though no acceptable individuals' BLL were identified in Iran, various studies have measured the BLL, comprising Moayedi et al. inquiry indicated that a person's BLL with natural exposer was 13.42 μg/dL, which had significant growth compared to the USA's BLL (less than 3 μg/dL) (Moayedi et al. 2008). Lead in the air is the only metal measured in Iran's National Ambient Air Quality Standard, by the average annual standard of 0.5μg/m^3 (Hassanvand et al. 2015). According to some research, previously Pb-contaminated soil (due to Pb-enriched fuel) is the major source of lead in many urban areas. According to Iran's Environmental Protection Organization (IEPO) standard, the amount of lead in residential, commercial, and agricultural areas' soil (acidic soils/pH less than 7) are 50, 200, and 50, respectively. Moreover, soil with a pH of more than 7 is 820, 2500, and 820 mg/kg soil (Organization Environmental Protection 2020).

In developing countries, fossil fuels, lead–acid battery, e-waste, lead-based paint, and unsanitary recycling of lead are sources of exposure to lead. In addition, lead-painted Chinese dolls, traditional medicines, and imported spices are international sources of lead-based pollutants (Golpayegani and Khanjani 2012). Also, recent studies reported the presence of lead in cosmetics, including lipstick and hair dyes (Sharafi et al. 2015).

The WHO estimates sources of lead exposure for children include food (47%), dust (45%), water (6%), and air (1%). Exposure to lead has gradually decreased by increasing food safety and control in the daily diet of people. However, children who have hand-mouth habits and behaviors are still directly exposed to dust (Han et al. 2018).

Studies have reported that the average BLL in the US population (2010), as well as Sweden (2013) and New York (2015) with natural exposure, was less than 1.5 μg/dL (Falq et al. 2011; Bjermo et al. 2013; Pollack et al. 2015). A study is carried out to determine the reference value (R.V.) of BLL with a sample size of 400 in the province of South Khorasan by Nakhaee et al. In this study, the mean of BLL (5.11 ± 7.41 μg/dL) was higher than the values determined by the CDC. In 13% of these subjects, BLL was reported higher than 10 μg/dL. The RV for BLL for men and women were 16 (95% CI, 10.13–15.96) μg/dL and 15 (95% CI, 9.81–14.45) μg/dL, respectively. The results of this study show that BLL was significantly higher in men than in women. The results of many studies around the world also confirm that men have higher BLL than women. Factors such as age, gender, hemoglobin, white blood cell count, and serum phosphorus concentration were the reason for this difference.

According to the results of this article, the reasons for the high level of lead in men's blood compared to women are as follows: more exposure of men due to work and presence in areas contaminated by lead. The higher estrogen level in young or pubertal women causes lead to be stored in their bones and released into the bloodstream at a slower rate. Also, the amount of hemoglobin in men's blood is higher than in women, which can affect BLL (Nakhaee et al. 2019). In the present study, the forest plot results confirm the higher BLL in men than women. Nevertheless, the pooled effect results show that there was not any significant difference between the mean BLL of men compared to women and the mean BLL of adults compared to children with (P-value, 0.377 and 0.355, respectively). There was not any significant difference between males and females ($P > 0.05$); the highest and lowest amount was related to students and homemakers, respectively (Moayedi et al. 2008). These results could be due to the used scale to measure the effect, characteristics of the design, and the methods that reviewed studies conducted. According to the result, the BLL of young people, especially up to 30 years old, is higher than middle-aged people. In the cross-sectional research by Moayedi et al. in Arak, Iran (2008), 1140 individuals > 10 years old were selected for the determination BLL in the general population. From the 1140 investigated residents, 463 individuals (40.5%) had BLL more than 10 μg/dL (range 0–66 μg/dL, mean 13.42 μg/dL) (Moayedi et al. 2008).

Conclusion

Regardless of pollution regulations, economic development will undoubtedly cause heavy metal exposure, especially lead, in developing countries. Since the main environmental route of exposure to lead is inhalation that causes serious health problems, regulations have demonstrated the effectiveness of restricting exposure to sources including petrol, paint, and plumbing, which can be a short-term precaution. The mean blood lead level is valuable information to determine the reference value so that this index could be the base of the regulations. Furthermore, identifying the main sources of lead as well as formulating economic development according to pollution regulations can be useful in reducing the health risks of lead exposure.

Acknowledgement The author would like to thank the support of the Tehran University of Medical Sciences.

Availability of data and materials Not applicable.

Author contributions **Nahid Khoshnamvand:** methodology, formal analysis, and writing—original draft. **Nahid Azizi:** review and editing. **Mohammad Sadegh Hassanvand:** conceptualization. **Mansour Shamsipour:** review and editing. **Vahide Oskoei: e**diting. **Kazem Naddafi:** conceptualization and supervision.

Declarations

Ethical approval Not applicable.

Consent to participate Not applicable.

Consent to publish Not applicable.

Competing interests Not applicable.

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