

Prevalence of Vitamin D Deficiency according to Climate Conditions among a Nationally Representative Sample of Iranian Adolescents: the CASPIAN-III Study

Roya Kelishadi¹, Mostafa Qorbani^{2,3}, *Mohammad Esmail Motlagh⁴, Ramin Heshmat³, Parinaz Poursafa⁵, *Maryam Bahreynian¹

¹Department of Pediatrics, Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran. ² Department of Community Medicine, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran. ³Department of Epidemiology, Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. ⁴Pediatrics Department, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. ⁵Department of Environmental Health, Environment Research Center, Research Institute for Primordial Prevention of Non-Communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract

Background: Sunlight is the main source of vitamin D; therefore, environmental factors might have an important role in the high prevalence of hypovitaminosis D in children. This study aimed to assess the vitamin D status according to the climate of the living area in a nationally representative sample of Iranian adolescents.

Material and Methods: This nationwide cross-sectional survey was performed among a representative sample of 1,095 adolescents aged 10-18 years, selected by multistage cluster sampling method from 27 provinces of Iran. Serum 25-hydroxyvitamin D [25(OH) D] concentrations were compared in inhabitants of humid-rainy, cold-mountainous, and sunny regions.

Results: Vitamin D deficiency was documented in 40% of participants including 40.70% of boys and 39.30% of girls. We found significant difference in 25(OH) D concentrations among participants living in the three different climates of the living area ($P < 0.05$). The median inter-quartile range (IQR) level for 25(OH)D was lower in humid-rainy climate: 11.40 (18.64). Hypovitaminosis D was more frequent in humid-rainy climate (42.30%), compared to other climates; this difference was more prominent in urban areas ($P < 0.05$). Boys living in various climates had significantly different levels of 25(OH) D ($P < 0.05$), however this figure was not significantly different for girls ($P > 0.05$). The highest frequency of hypovitaminosis D (45.2%) was documented among boys living in humid-rainy regions.

Conclusion: The high prevalence of hypovitaminosis D, notably among inhabitants of humid-rainy region underscores the necessity of implementing national preventive strategies. This is of great importance especially in regions with lower exposure to sunlight.

Key Words: Children and adolescents, Climate, Iran, Vitamin D deficiency.

*Please cite this article as: Kelishadi R, Qorbani M, Motlagh ME, Heshmat R, Poursafa P, Bahreynian M. Prevalence of Vitamin D Deficiency according to Climate Conditions among a Nationally Representative Sample of Iranian Adolescents: the CASPIAN-III Study. *Int J Pediatr* 2016; 4(6): 1903-1910.

*Corresponding Authors:

Mohammad Esmail Motlagh and Maryam Bahreynian, Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non Communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran.

Email: bahreynian@hlth.mui.ac.ir and mohammad-motlagh1389@yahoo.com

Received date Feb23, 2016; Accepted date: Mar 22, 2016

1- INTRODUCTION

Vitamin D is a fat-soluble vitamin that is produced in sun-exposed skin, and is obtained from dietary intake in lower amounts. Liver and kidneys are two important organs that activate vitamin D as 1,25-dihydroxy vitamin D₃ (1). Vitamin D plays a key role in maintaining the mineral and skeletal homeostasis. Further associations of vitamin D status and risk of several chronic diseases as cardiovascular disease, multiple sclerosis, and inflammatory disorders are well documented (2-5).

Vitamin D deficiency (hypovitaminosis D) is a major public health challenges in both developed and developing countries (6-9). The consequences related to vitamin D deficiency include improper bone development and increased risk of some cancers, cardiovascular disease, type 1 diabetes and other autoimmune diseases (1, 10).

The prevalence of hypovitaminosis D varies significantly among different studies because of the diversity in populations studied and in the cut-offs used (11). It has been estimated that 30-50% of both children and adults living in the US, Canada, Australia, New Zealand, Europe and Asia are vitamin D deficient (11-16).

In spite of the important role of sunlight exposure in vitamin D synthesis, studies have indicated high prevalence of vitamin D deficiency in sunny areas located in the Middle-East countries such as Saudi Arabia, Qatar, United Arab Emirates, India, Turkey, and Iran (1, 11, 13, 14, 17). A remarkably high rate of vitamin D deficiency is reported among 79.6% of 20-69- year- old Iranian population (9) and 46.2% of 14-18-year-old adolescents (18). Various prevalence rates of vitamin D deficiency are reported among different age-groups of Iranian population, but all of them confirm high prevalence of

hypovitaminosis D in different populations(8, 9, 18-20).

Understanding the vitamin D status of different age-groups in a country and in a wide range of climate conditions of a community is necessary for development of new and practical programs to improve general health. Therefore, the present study was performed to investigate the prevalence of vitamin D deficiency among a nationally representative sample of Iranian adolescents living in areas with different climate conditions in Iran.

2-2. Measuring tools

2-1. Study design and population

This nationwide cross-sectional study was conducted as a sub-study of the third phase of a national school-based surveillance program entitled Childhood Adolescence Surveillance and Prevention of Adult Non-communicable disease (CASPIAN) study, in Iran. More details on the study are published elsewhere (21). Briefly, the CASPIAN-III survey was performed on a stratified multi-stage probability sample of 5,625 children and adolescents, aged 10-18 years, living in urban and rural areas of 27 provinces in Iran.

2-2. Measuring tools

Of 5,625 participants aged 10-18 years, who were selected by stratified multistage random sampling method from urban and rural areas of 27 provinces in Iran, 1,095 students were selected through systematic random method to measure their serum 25(OH)D concentration. After complete explanation of the study, written informed consent was obtained from parents and oral assent from students.

2-3. Methods

Vitamin D levels were measured using blood samples collected after a 12-hour overnight fasting. Serum concentration of 25(OH)D was analyzed quantitatively using direct competitive immunoassay

chemiluminescence method and LIASON® 25 OH vitamin D assay TOTAL (DiaSorin, Inc.), with a coefficient of variation (CV) of 9.8%. Serum 25(OH)D concentration of less than 30ng/mL was considered as vitamin D deficiency, and vitamin D insufficiency was defined as a 25(OH)D concentration of 20 to 30 ng/ml (22). Country classification into sub-national regions was according to a previous study. In which, the sub-national areas were defined based on the combination of different factors including their geographical situation (23). The regions were categorized as humid-rainy climate (North-Northeast), cold-mountainous (West), and sunny climate (Central) parts.

2-4. Data analyses

Normal distribution of serum 25(OH)D concentration was assessed using Kolmogorov-smirnov test and because of the lack of normality, the concentrations are presented as median and inter-quartile range (IQR), and were compared across regions by using Kruskal-Wallis test. Prevalence of vitamin D deficiency and insufficiency across regions was assessed using Pearson Chi-square test. Data were analyzed using survey data method in the Statacrop, 2011 (Stata Statistical Software: Release 12. College Station, TX: Stata Crop LP.Package). $P < 0.05$ was considered as statistically significant.

2-5. Ethical considerations

The ethical committees of Tehran and Isfahan University of Medical Sciences approved the main study, and the current sub-study was approved by the research and ethics committee of Isfahan University of Medical Sciences (ID Number: 190149).

3- RESULTS

This cross-sectional nationwide survey was conducted among 1,095 Iranian school

students (48.1% girls, 67.0% urban), with mean \pm standard deviation (SD) age of 14.74 ± 2.60 years. More than 90% of the study participants were from public schools.

Table.1 demonstrates the median and IQR of vitamin D at national and regional levels according to gender and the living area. The median (IQR) for vitamin D concentration was 13.00 (20.56) ng/ml at national level. The median (IQR) of vitamin D concentration was 13.15 (17.41) for urban and 12.45 (20.99) for rural inhabitants. Although the humid-rainy climate (North, North-eastern regions) showed lower levels of 25(OH) D than cold-mountainous (West) and sunny (Central) climates, it was not statistically significant ($P = 0.54$).

Table.2 shows the prevalence of vitamin D insufficiency and deficiency at national and regional levels. In total, the prevalence of vitamin D deficiency was 40%, including 40.70% of boys and 39.30% of girls. Among urban students, 42.50% were vitamin D deficient, this figure was 40% for students living in rural areas. We found significant difference in 25(OH) D levels between three different climates ($P = 0.003$). The highest prevalence of vitamin D deficiency was observed in humid-rainy climate (42.30%) followed by cold-mountainous (42.19%) and sunny (35.31%) climate, which was statistically significant ($P = 0.003$). The prevalence of vitamin D deficiency in urban inhabitants of sunny climate (Central) was significantly lower than urban inhabitants of other regions ($P = 0.001$). Moreover, the prevalence of vitamin D deficiency in boys living in sunny climate (Central) was significantly lower than boys in other regions ($P = 0.04$). The lowest and highest frequency of vitamin D deficiency was documented among boys living in sunny (35.32%) and humid-rainy regions (45.26%), respectively.

Table 1: Median (IQR) of 25(OH)D concentration of Iranian adolescents at national and regional levels by gender and living region: the CASPIAN-III study

Vitamin D concentration					
Regions	North-Northeast (Humid-rainy)	West (Mountainous)	Central (Sunny)	National	P-value
Variables	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	
Boys	10.85 (18.77)	15.70 (25.54)	13.20 (17.18)	12.70 (21.80)	0.27
Girls	13.60 (18.32)	11.90 (20.93)	13.80 (17.97)	13.20 (19.33)	0.53
Urban	11.40 (16.52)	15.70 (25.41)	14.10 (16.82)	13.15 (17.41)	0.11
Rural	13.90 (23.58)	12.30 (19.96)	12.50 (19.03)	12.45 (20.99)	0.46
Total	11.40 (18.64)	13.55 (23.74)	13.50 (17.40)	13.00 (20.56)	0.54

IQR: Inter quartile range, 25th -75th**Table 2.** Vitamin D status of adolescents at national and regional level by gender and living area: the CASPIAN-III study

Regions						
Variables		North-Northeast (humid-rainy)	West (mountainous)	Central (sunny)	National	P-value
		N (%)	N (%)	N (%)	N (%)	
Boys	Deficient	86 (45.26)	80 (41.03)	65 (35.52)	231 (40.70)	0.04
	Insufficient	66 (34.74)	61 (31.28)	81 (44.26)	208 (36.60)	
	Sufficient	38 (20.00)	54 (27.96)	37 (20.22)	129 (22.70)	
Girls	Deficient	65 (38.92)	82 (43.39)	60 (35.09)	207 (39.30)	0.10
	Insufficient	68 (40.72)	66 (34.92)	84 (49.12)	218 (41.40)	
	Sufficient	34 (20.36)	41 (21.69)	27 (15.79)	102 (19.40)	
Urban	Deficient	109 (42.58)	111 (41.11)	64 (30.77)	284 (38.70)	0.001
	Insufficient	101 (39.45)	88 (32.59)	106 (50.96)	295 (40.20)	
	Sufficient	46 (17.97)	71 (26.30)	38 (18.27)	155 (21.10)	
Rural	Deficient	42 (41.58)	51 (44.74)	60 (41.38)	153 (42.50)	0.52
	Insufficient	33 (32.67)	39 (34.21)	59 (40.69)	131 (36.40)	
	Sufficient	26 (25.74)	24 (21.05)	26 (17.93)	76 (21.10)	
Total	Deficient	151 (42.30)	162 (42.19)	125 (35.31)	438 (40.00)	0.003
	Insufficient	134 (37.54)	127 (33.07)	165 (46.61)	426 (38.90)	
	Sufficient	72 (20.17)	95 (24.74)	64 (18.08)	231 (21.10)	

Data are presented as number (%)

4- DISCUSSION

This study revealed significant difference in 25(OH)D levels between three diverse climates, with the highest frequency of hypovitaminosis D observed among boys living in humid-rainy climate, in Iran.

Results of previous studies in Iran reported relatively high prevalence of vitamin D deficiency among different age groups (8, 17-19). In these studies, high-school students, pregnant women, and newborns were the most vulnerable groups for hypovitaminosis D (8, 19, 20).

Vitamin D deficiency is recognized as a widespread disorder among different populations because of the lack of sufficient sunlight exposure and/or insufficient dietary intakes (24-26). In addition to the large number of vitamin D functions, there are several non-skeletal roles of vitamin D including modulation of immune system (27), increasing insulin production, increment of myocardial contractility and inhibition of rennin system (1, 28). Thus, vitamin D deficiency might lead to increase the risk of immune and non-immune disorders such as type-1 diabetes, rheumatoid arthritis and congestive heart failure (1).

Determinants of vitamin D levels among different age groups in a country and in diverse climates seem necessary and might have useful implications in practice for general health. In our study, similar patterns of vitamin D deficiency were documented among boys and girls. It might represent the other causes leading to vitamin D deficiency rather than gender differences such as clothing style and exposure to sunlight. Our findings are consistent with another study that found a high prevalence of vitamin D deficiency among Iranian adults (17).

In the present study, we found the highest frequency of vitamin D deficiency among inhabitants of humid-rainy climate. This

region is almost all days rainy, therefore limited exposure to sunlight might explain this higher frequency compared to other climates. As the dietary habits in different parts of the country have the same pattern, the current finding underscores the role of environmental factors in the high prevalence of hypovitaminosis D in Iran.

A growing body of evidence exists on the high prevalence of vitamin D deficiency at global level (29-31). Despite different causes of vitamin D deficiency, diverse methods and measurements of serum vitamin D levels, air pollution might be considered as a possible leading cause of vitamin D insufficiency and/or deficiency.

Previous studies have demonstrated the effect of atmospheric pollution on vitamin D concentration (32, 33). Evidence suggests that increased air pollution as a result of industrialization and urbanization might absorb the solar ultraviolet B (UVB) photons, thus leading to reduced synthesis of cutaneous vitamin D (33-35). During sunlight exposure, the UVB photons (290-315 nm) go through the skin, where they cause the photolysis of 7-dehydrocholesterol to cholecalciferol. Latitude, seasonal changes, and time of day as well as atmospheric ozone pollution affect the number of UVB photons that reach the earth's surface, and thus, alter the cutaneous production of cholecalciferol (33, 34). Air pollution has been a serious environmental problem, and known as a global health threat in developed countries (36, 37), and also, developing countries such as Iran (38, 39). Thus, as documented in some previous studies it seems that a relatively high prevalence of vitamin D deficiency in central parts of our country, i.e. sunny climate, is due to the atmospheric air pollution. Some previous studies in Iran documented higher prevalence of hypovitaminosis D in children and cord blood of pregnant women living in sunny but air-polluted regions (40). This is in line with findings

of studies in sunny countries located in Africa and the Middle East (7). Several features of the current study make its results valuable and practical. The data were obtained from a large nationally representative sample of Iranian school-aged children, both genders and inhabitants of different climates. However, due to its cross-sectional nature, causality could not be inferred. Another possible limitation is that a single serum 25 (OH)D concentration might not accurately reflect vitamin D status for the whole year, however in all regions, blood samples were obtained at the same time, and the findings are compared in regions with different climates.

5- CONCLUSION

The prevalence of hypovitaminosis D is considerably high in Iranian adolescents, notably in inhabitants of humid-rainy climate region. Although the prevalence of vitamin D deficiency was similar in urban and rural areas, the importance of environmental factors should be highlighted in this regard, and implementing preventive strategies are recommended at national level by focusing on vulnerable groups.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENT

The authors would like to thank the large team working, all students and school principals.

8- SOURCE OF FUNDING

The study was funded by Isfahan University of Medical Sciences (ID Number: 190149).

9- REFERENCES

1. Holick MF. Vitamin D deficiency. *The New England journal of medicine*. 2007 Jul 19;357(3):266-81. PubMed PMID: 17634462. Epub 2007/07/20. eng.
2. Skaaby T, Husemoen LL, Borglykke A, Jorgensen T, Thuesen BH, Pisinger C, et al. Vitamin D status, liver enzymes, and incident liver disease and mortality: a general population study. *Endocrine*. 2014 Sep;47(1):213-20. PubMed PMID: 24272594. Epub 2013/11/26. eng.
3. Skaaby T, Husemoen LLN, Pisinger C, Jørgensen T, Thuesen BH, Fenger M, et al. Vitamin D status and changes in cardiovascular risk factors: a prospective study of a general population. *Cardiology*. 2012;123(1):62-70.
4. Skaaby T, Husemoen LLN, Pisinger C, Jørgensen T, Thuesen BH, Fenger M, et al. Vitamin D status and incident cardiovascular disease and all-cause mortality: a general population study. *Endocrine*. 2013;43(3):618-25.
5. Husemoen LL, Skaaby T, Thuesen BH, Jorgensen T, Fenger RV, Linneberg A. Serum 25(OH)D and incident type 2 diabetes: a cohort study. *European journal of clinical nutrition*. 2012 Dec;66(12):1309-14. PubMed PMID: 23031851. Epub 2012/10/04. eng.
6. Duval GT, Brangier A, Barre J, Launay CP, Beauchet O, Annweiler C. Vitamin D Deficiency and Incident Onset of Orthostatic Hypotension in Older Adults: Preliminary Results from the 'MERE' Study. *Journal of the American Geriatrics Society*. 2015 Jun;63(6):1245-7. PubMed PMID: 26096400. Epub 2015/06/23. eng.
7. Green RJ, Samy G, Miqdady MS, El-Hodhod M, Akinyinka OO, Saleh G, et al. Vitamin D deficiency and insufficiency in Africa and the Middle East, despite year-round sunny days. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2015 Jul;105(7):603-5. PubMed PMID: 26447257. Epub 2015/10/09. eng.
8. Salek M, Hashemipour M, Aminorroaya A, Gheiratmand A, Kelishadi R, Ardestani P, et al. Vitamin D deficiency among pregnant women and their newborns in Isfahan, Iran. *Experimental and clinical endocrinology & diabetes*. 2008;116(6):352.
9. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M, et al. Vitamin D deficiency and causative factors in

the population of Tehran. *BMC Public health*. 2004;4(1):38.

10. Pacifici GM. Effects of Vitamin D in Neonates and Young Infants. *International Journal of Pediatrics*. 2016;4(1):1273-85.

11. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocrine reviews*. 2001;22(4):477-501.

12. Holick MF, editor High prevalence of vitamin D inadequacy and implications for health. *Mayo Clinic Proceedings*; 2006;81(3):353-73. Elsevier.

13. Boonen S, Bischoff-Ferrari H, Cooper C, Lips P, Ljunggren O, Meunier P, et al. Addressing the musculoskeletal components of fracture risk with calcium and vitamin D: a review of the evidence. *Calcified tissue international*. 2006;78(5):257-70.

14. Bakhtiyarova S, Lesnyak O, Kyznesova N, Blankenstein M, Lips P. Vitamin D status among patients with hip fracture and elderly control subjects in Yekaterinburg, Russia. *Osteoporosis international*. 2006;17(3):441-6.

15. Sharawat I, Sitaraman S, Dawman L. Prevalence of Vitamin D Deficiency among Healthy School Children in Jaipur District, Rajasthan, India. *International Journal of Pediatrics*. 2015;3(4.2):801-.

16. Shamsian AA, Rezaee SA, Rajabian M, Taghizade Moghaddam H. Serum 25-hydroxyvitamin D Levels in Patients Referred to Clinical Laboratories in Various Parts of Mashhad-Northeastern Iran. *International Journal of Pediatrics*. 2015;3(3.2):691-7.

17. Hovsepian S, Amini M, Aminorroaya A, Amini P, Iraj B. Prevalence of vitamin D deficiency among adult population of Isfahan City, Iran. *Journal of health, population, and nutrition*. 2011;29(2):149.

18. Azizi F, Rais Zadeh F, Mir Saeed Ghazi A. Vitamin D deficiency in a group of Tehran Population. 2000.

19. Moussavi M, Heidarpour R, Aminorroaya A, Pournaghshband Z, Amini M. Prevalence of vitamin D deficiency in Isfahani

high school students in 2004. *Hormone Research in Paediatrics*. 2005;64(3):144-8.

20. Shahla A, Charehsaz S, Talebi R, Omrani M. Vitamin D deficiency in young females with musculoskeletal complaints in Urmia, northwest of Iran. *IJMS*. 2005;30(2):88-90.

21. Kelishadi R, Heshmat R, Motlagh ME, Majdzadeh R, Keramatian K, Qorbani M, et al. Methodology and Early Findings of the Third Survey of CASPIAN Study: A National School-based Surveillance of Students' High Risk Behaviors. *International journal of preventive medicine*. 2012 Jun;3(6):394-401. PubMed PMID: 22783465. Pubmed Central PMCID: PMC3389436. Epub 2012/07/12.

22. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *The Journal of clinical endocrinology and metabolism*. 2011 Jul;96(7):1911-30. PubMed PMID: 21646368. Epub 2011/06/08. eng.

23. Farzadfar F, Danaei G, Namdaritabar H, Rajaratnam JK, Marcus JR, Khosravi A, et al. National and subnational mortality effects of metabolic risk factors and smoking in Iran: a comparative risk assessment. *Population health metrics*. 2011;9(1):55. PubMed PMID: 21989074. Pubmed Central PMCID: PMC3229448. Epub 2011/10/13. eng.

24. O'Sullivan M, Nic Suibhne T, Cox G, Healy M, O'Morain C. High prevalence of vitamin D insufficiency in healthy Irish adults. *Irish journal of medical science*. 2008 Jun;177(2):131-4. PubMed PMID: 18274816. Epub 2008/02/16. eng.

25. Bener A, Alsaied A, Al-Ali M, Hassan AS, Basha B, Al-Kubaisi A, et al. Impact of lifestyle and dietary habits on hypovitaminosis D in type 1 diabetes mellitus and healthy children from Qatar, a sun-rich country. *Annals of nutrition & metabolism*. 2008;53(3-4):215-22. PubMed PMID: 19077420. Epub 2008/12/17. eng.

26. Marwaha RK, Tandon N, Reddy DR, Aggarwal R, Singh R, Sawhney RC, et al. Vitamin D and bone mineral density status of healthy schoolchildren in northern India. *The*

- American journal of clinical nutrition. 2005 Aug;82(2):477-82. PubMed PMID: 16087996. Epub 2005/08/10. eng.
27. DeLuca HF. Overview of general physiologic features and functions of vitamin D. *The American journal of clinical nutrition*. 2004 Dec;80(6 Suppl):1689S-96S. PubMed PMID: 15585789. Epub 2004/12/09. eng.
28. Kelishadi R, Farajzadegan Z, Bahreynian M. Association between vitamin D status and lipid profile in children and adolescents: a systematic review and meta-analysis. *International journal of food sciences and nutrition*. 2014 Jun;65(4):404-10. PubMed PMID: 24524677. Epub 2014/02/15. eng.
29. Lee YA, Kim HY, Hong H, Kim JY, Kwon HJ, Shin CH, et al. Risk factors for low vitamin D status in Korean adolescents: the Korea National Health and Nutrition Examination Survey (KNHANES) 2008-2009. *Public Health Nutr*. 2014 Apr;17(4):764-71. PubMed PMID: 23462341. Epub 2013/03/07.
30. Riaz H, Finlayson A, Bashir S, Hussain S, Mahmood S, Malik F, et al. Prevalence of Vitamin D deficiency in Pakistan; implications for the future. *Expert review of clinical pharmacology* 2016;9(2):329-38;9.
31. Faghih S, Abdolazadeh M, Mohammadi M, Hasanzadeh J. Prevalence of vitamin d deficiency and its related factors among university students in shiraz, iran. *International journal of preventive medicine*. 2014 Jun;5(6):796-9. PubMed PMID: 25013702. Pubmed Central PMCID: PMC4085935. Epub 2014/07/12. eng.
32. Agarwal KS, Mughal MZ, Upadhyay P, Berry JL, Mawer EB, Puliyl JM. The impact of atmospheric pollution on vitamin D status of infants and toddlers in Delhi, India. *Archives of disease in childhood*. 2002 Aug;87(2):111-3. PubMed PMID: 12138058. Pubmed Central PMCID: PMC1719192. Epub 2002/07/26. eng.
33. Holick MF. Environmental factors that influence the cutaneous production of vitamin D. *The American journal of clinical nutrition*. 1995 Mar;61(3 Suppl):638S-45S. PubMed PMID: 7879731. Epub 1995/03/01. eng.
34. Holick MF. Photosynthesis of vitamin D in the skin: effect of environmental and life-style variables. *Federation proceedings*. 1987 Apr;46(5):1876-82. PubMed PMID: 3030826. Epub 1987/04/01. eng.
35. Calabrese EJ. The influence of ambient ozone on the incidence of bone fractures especially among the elderly. *Medical hypotheses*. 1979 Feb;5(2):201-7. PubMed PMID: 459973. Epub 1979/02/01.
36. Hicken MT, Adar SD, Hajat A, Kershaw KN, Do DP, Barr RG, et al. Air Pollution, Cardiovascular Outcomes, and Social Disadvantage: The Multi-ethnic Study of Atherosclerosis. *Epidemiology (Cambridge, Mass)*. 2016 Jan;27(1):42-50. PubMed PMID: 26618771. Epub 2015/12/01. eng.
37. Thurston GD, Burnett RT, Turner MC, Shi Y, Krewski D, Lall R, et al. Ischemic Heart Disease Mortality and Long-Term Exposure to Source-Related Components of U.S. Fine Particle Air Pollution. *Environmental health perspectives*. 2015 Dec 2. PubMed PMID: 26629599. Epub 2015/12/03. Eng. *Environ Health Perspect*. 2015 Dec 2. [Epub ahead of print]
38. Poursafa P, Kelishadi R, Ghasemian A, Sharifi F, Djalalinia S, Khajavi A, et al. Trends in health burden of ambient particulate matter pollution in Iran, 1990-2010: findings from the global burden of disease study 2010. *Environmental science and pollution research international* 2015; 22(23):18645-53.
39. Khamutian R, Najafi F, Soltanian M, Shokoozadeh MJ, Poorhaghighat S, Dargahi A, et al. The association between air pollution and weather conditions with increase in the number of admissions of asthmatic patients in emergency wards: a case study in Kermanshah. *Medical journal of the Islamic Republic of Iran*. 2015;29:229. PubMed PMID: 26478887. Pubmed Central PMCID: PMC4606958. Epub 2015/10/20. eng.
40. Kelishadi R, Moeini R, Poursafa P, Farajian S, Yousefy H, Okhovat-Souraki AA. Independent association between air pollutants and vitamin D deficiency in young children in Isfahan, Iran. *Paediatrics and international child health* 2014;34(1):50-5. PubMed PMID: 24090719. Epub 2013/10/05. eng.