

HUMAN HEALTH RISK (HHR) OF NITRATES IN THE GROUNDWATER OF ABUWAJNAH VILLAGE, TAL AFAR DISTRICT. IRAQ

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ABSTRACT

The study was carried on Abu Wajnah village of Tal Afar district, which depends mainly on groundwater as a source of drinking water to know the health safety of this water on the health of consumers, especially the risks resulting from the presence of nitrate ions in the water, considering that the local people are engaged in agriculture and ranching, fourteen wells were identified for collecting water samples and the concentration of nitrate ions was determined with a Human Health Hazards (HHR) of nitrates calculated according to international standard methods. Fortunately, the results of the study registered that there is no risk to nitrates in drinking water for the health of consumers because the values of hazard quotient of nitrate (HQ_{nitrate} or HQ for different age groups) ranged between (0.0228 to 0.1125) and thus it is within the limits allowed globally (less than 1), they attributed this decrease in values to the decrease in the values of chronic daily intake (CDI) of studied water, which fluctuated between (0.0142 to 0.1800). They attributed this decrease in values to the low concentration of nitrate ions, which was reflected in the values of chronic daily intake (CDI) of studied water which fluctuated between (0.362 to 3.20) ppm.

KEYWORD: Human health hazards, HHR, NO_3 Hazards, Water quality.

INTRODUCTION

Despite the damage caused by the high levels of nitrate and nitrite compounds in drinking water and foods, but the few concentrations of them have benefits for human health, according to recent studies. Assuming Al-Hamdany et al, (2020) that the inorganic compounds of nitrates and nitrites present in drinking water or vegetables have a positive effect on human health through biological interactions of nitrate compounds and by-products of secondary reactions by bacteria in the oral cavity to produce nitrite and nitric oxide etc.

These products have an effective and preventive role for the heart and blood vessels (Zuckerbraun et al, 2017). Likewise, nitrogen oxide (NO) as free radical plays an important role in regulating blood pressure with vasodilation and tissue protection properties, also, signalling is vasoprotective in the regulation of pulmonary arterial hypertension (PAH) (Zuckerbraun et al, 2011). However, the high concentrations of nitrate and nitrite ions over the permissible limits by (WHO, 2011) can cause severe dangerous effects on human health. Long-term exposure to nitrate compounds and their reduction to nitrite ions in the oral cavity by bacteria, and the interaction of these ions with secondary

amines or amides from their presence in the stomach to form N-Nitroso Compounds (NOC), and most of these compounds cause dangerous diseases. Like methemoglobinemia or blue baby syndrome (Met Hb), which is caused by the oxidation of ferrous in hemoglobin to ferric state, and its transformation into methemoglobin which cannot carry oxygen molecules and when it is high it causes blue blood and hypoxia in body tissues and severe cases lead to death (Breda et al, 2019), this is confirmed by studies conducted in the USA for more than fifty years, which indicated that the main cause of methemoglobinemia (Met Hb) is that the high level of nitrates in drinking water above the permitted levels (45 ppm) and 80% of infants who have been exposed to nitrate levels in drinking water exceed the permissible limit suffer from these health risks, as shown in picture (1) likewise, prolonged exposure to nitrates in drinking water above the permissible maximum level can lead to diuresis and spleen bleeding (Ahmed et al, 2019).

For pregnant women, some researchers have suggested that the placenta membrane (barriers) is effective in separating the blood circulation between the mother and the fetus after the first trimester (1st trimester), thus preventing methemoglobin molecules from crossing to the fetus, while others suggested transferring NO_2 to the

fetus via an active transfer system as a result of observing fetal levels of nitrites in the plasma compared to their levels in the blood of the mother (Manassaram *et al.*, 2006). Reports also indicate that several cases of repeated abortions for pregnant women in LaGrange, Indiana due to the use of wells with high concentrations of nitrates above (MCL), also, there is a relationship between these levels, pregnancy complications, birth defects, and an increased risk of cancer (CDC, 1996; Juntakut *et al.*, 2020). Besides, the high concentration of nitrates can adversely affect the health of pregnant women and those adults with a rare metabolic phosphate

dehydrogenase deficiency (WHO, 2017). Other health risks have been reported for exposure to elevated levels of nitrate that carries a risk of human genetic toxicity due to the internal formation of carcinogenic N-nitroso compounds. Resulting from the interaction of nitrate-derived nitrite *in vivo* with amines and amides to form N-nitroso compounds. From experiments and tests, about 300 N-nitroso compounds (NOCs) were found to search for carcinogenicity in experimental animals; 85% of 209 nitrosamines and 92% of 86 nitrosamides had carcinogenic effects (Vermeer *et al.*, 1998).



Pictures (1): Show symptoms of the blue baybe syndrome. (net)

Also, Yu *et al.* (2020) indicated that there is a relationship between nitrate and nitrite consumption and the risk of non-Hodgkin's lymphoma (NHL), and the risk of the development of NHL increases in the future for each additional microgram of nitrite consumed daily. Non-Hodgkin's lymphoma (NHL) is a group of lymphomas that develop mainly from cells in the lymph nodes. Recently, the NHL has been classified into over forty forms based on histopathological and histological features (WHO, 2011). Especially for high-risk subspecies (e.g. immunoblast, lymphoma, Burkitt lymphoma and lymphoblastic lymphoma), Studies show that human exposure to (NOCs) compounds increases the risk of stomach, oesophageal, and bladder cancer (Al-Hamdany *et al.*, 2020 and Al-Saffawi, 2019).

Therefore, the current study came to assess the human health risks of nitrate in the groundwater for the village of Abu-Wajnah, Tal Afar District. As the main source of water in the village.

MATERIALS AND METHODS

I. Description of the study area

The village of Abu Wajnah is located northwest of Mosul city, the Tal Afar district, Nineveh Governorate, on a longitude (36°41'28") north. and latitude (42°37'22") E, 90 km away from the city and is characterized by the weather of the area is hot dry in summer and cold rainy in winter. The average annual rainfall is 450 mm (Al-Mashhdany *et al.*, 2020) and most of its residents work in agriculture and ranching depending on the groundwater for different uses because the area is far from rivers. Where 14 random wells were chosen in the village, with depths ranging between (18-30) meters, nine of them which are classified as deep wells and the rest are shallow. (Al-Shanona *et al.*, 2018) as shown in (Fig. 1).

II. Geology of the study area

There are many geological formations in the study area, such as the Plaspi (Upper Middle Eosin) containing limestone. and the formation of Al Fa'tha (Middle-

Miocene) containing limestone and gypsum rocks ($\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$), anhydrite (CaSO_4) and evaporated salts in addition to marl with sandy or clay layers etc. and the formation of anjana consisting of sandy and alluvial layers in succession and sometimes clay and the formation of Miqdadiya (pliocene). Finally, sediments dating back to the quaternary period, consisting of gravel, sand, silt and clay appear in the studied area.

III. Sampling and Methodolgy

Groundwater samples were collected during the dry season (4 replicates per well) using clean polyethene bottles that were washed with the sample water before it filling, using standard methods to collect and determine nitrate concentration in water samples by the Ultraviolet

Spectrophotometric Screening Method along with the 220 and 270 nm (APHA, 2017).

IV. Assessment of human health risk (HHR) of nitrate via drinking water

HHR was evaluated, according to the US Environmental Protection Agency (USEPA), which is widely used to assess the nitrate human health risks (Adimalla and Wu, 2019; Adimalla and Li, 2019). The nitrate concentration was chosen in the present study to evaluate HHR due to its serious effects on human health. The chronic daily intake (CDI) and hazard quotient (HQ) or the hazard index resulting from nitrate ion ($\text{HI}_{\text{nitrate}}$) were calculated by following equations (Zhang et al, 2019):

$$\text{CDI} = \text{Cw} \times \text{IR} \times \text{EF} \times \text{ED} / \text{Bw} \times \text{AT}$$

$$\text{HI (nitrate)} = \text{HQ} = \text{CDI} / \text{RfD}$$

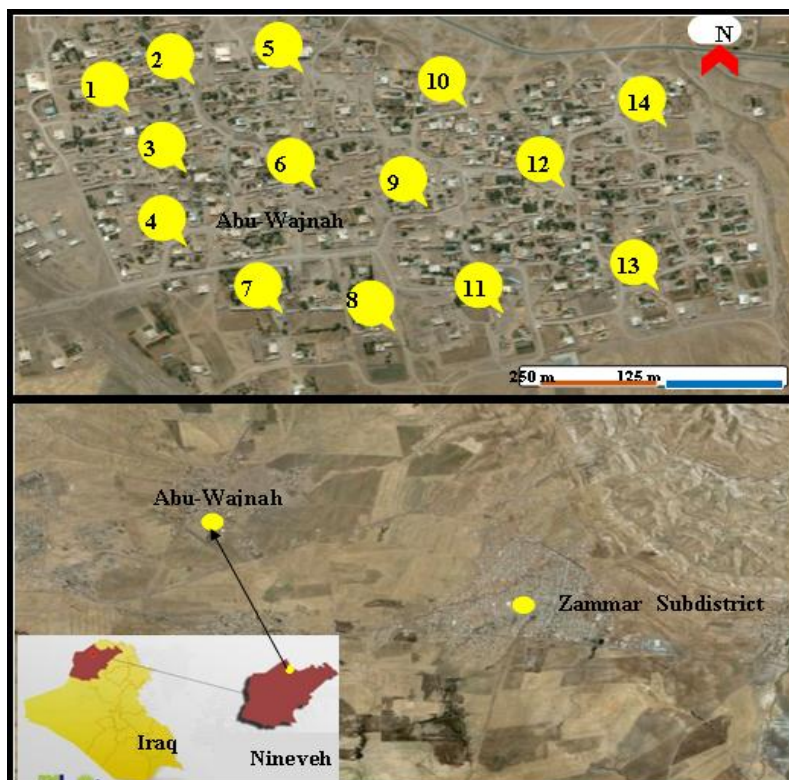


Fig. (1): Wells sites studied for the village of Abu Wajnah, Nineveh Governorate.

Where CDI is the chronic daily intake (mg/kg day) and Cw represents the concentration of nitrates in drinking water (ppm). Daily average ingestion of water (IR) for different ages of adults, children and infants in litres, ED represents the duration of exposure in years. For the study area, the local population relies on groundwater for drinking purposes. Therefore, the frequency of exposure (EF) is 365 days/ year. Bw: Average body weight in kg, mean time values (ET) in days, RfD represents the reference dose of nitrates (1.6 mg / kg /d) and these data are obtained from Risk Information Systems (US.EPA, 2014; Zhang et al, 2019). If HI (HQ) values override one, it is considered as an unbearable peril of adverse effects on health, but it is equal to less than one, then the drinking water is considered as within the accepted limit (Adimalla and Wu, 2018)

RESULTS AND DISCUSSION

The main sources of water pollution, whether surface or groundwater with nitrates are agricultural fertilizers, human and animal waste, wastewater etc. The concentrations of nitrate ions in groundwater are often much higher than in surface water. Fortunately, the concentrations of nitrate ions in groundwater, especially on Nineveh Governorate, Iraq are relatively few, as the results are shown in Table (1) indicate that the concentration of nitrate ions in the Abu Wajnah region fluctuated between (0.362 ± 0.288 to 3.200 ± 0.993) ppm and a rate ranging between 0.679 to 1.638 and is much less than the universally permissible limits (WHO, 2017).

Table (1): Average and range of nitrate ion concentrations for groundwater in Abu Wajna village (ppm).

Wells	Min.	Max.	Mean	± Sd
1	0.812	2.700	1.638	0.740
2	0.671	3.100	1.605	0.939
3	0.709	1.760	1.222	0.400
4	0.746	2.400	1.512	0.680
5	0.441	1.986	1.189	0.628
6	0.638	3.200	1.599	0.993
7	0.756	1.400	1.164	0.289
8	0.923	1.278	1.067	0.152
9	0.630	1.261	0.868	0.279
10	0.728	1.286	0.945	0.244
11	0.450	1.120	0.735	0.283
12	0.510	2.274	1.266	0.644
13	0.718	1.776	1.096	0.406
14	0.362	1.145	0.679	0.288

These results are relatively close to the results obtained by Al-Saffawi et al (2020a) when they studied the groundwater of Al-Kask subdistrict, west of Mosul, Iraq, which ranged between (0.28 to 2.90) ppm, while it was less than the results obtained by Talaat et al (2019) for the concentration of nitrate ions in the groundwater to the left side of the city of Mosul, which reached to (12.30)

ppm. The important source of groundwater pollution with nitrate ions in the studied area, which are fertilizers used for agricultural purposes. especially the incorrect and improper use of nitrogenous fertilizers with the spread of animal manure (livestock) and thus the possibility of them reaching the groundwater (Jaafer and Al-Saffawi, 2020).

Table (2): Results of the chronic daily intake (CDI) and hazard quotient of nitrates ($HI_{\text{nitrate}} = HQ$) for different age groups in the village of Abu-Wajnah.

Age Years		< 1.0	6.0 -11	11-16	18 -21	21-65	> 65
Wells							
1	CDI	0.1800	0.0738	0.0550	0.0567	0.0605	0.0559
	HQ	0.1125	0.0461	0.0344	0.0354	0.0378	0.0349
2	CDI	0.1764	0.0723	0.0539	0.0556	0.0593	0.0548
	HQ	0.1103	0.0452	0.0337	0.0348	0.0371	0.0342
3	CDI	0.1343	0.0551	0.0410	0.0423	0.0451	0.0417
	HQ	0.0839	0.0344	0.0257	0.0264	0.0282	0.261
4	CDI	0.1662	0.0681	0.0508	0.0523	0.0558	0.0516
	HQ	0.1039	0.0426	0.0317	0.0327	0.0349	0.0323
5	CDI	0.1307	0.0536	0.0399	0.0412	0.0439	0.0406
	HQ	0.0817	0.0335	0.0250	0.0257	0.0274	0.0254
6	CDI	0.1757	0.0720	0.0537	0.0554	0.0591	0.0546
	HQ	0.1098	0.0450	0.0336	0.0346	0.0369	0.0341
7	CDI	0.1279	0.0524	0.0391	0.0403	0.0430	0.0397
	HQ	0.0799	0.0328	0.0244	0.0252	0.0269	0.0248
8	CDI	0.1173	0.0481	0.0358	0.0369	0.0394	0.0364
	HQ	0.0733	0.0300	0.0224	0.0231	0.0246	0.02227
9	CDI	0.0954	0.0391	0.0292	0.0301	0.0321	0.0296
	HQ	0.0596	0.0244	0.0182	0.0188	0.0200	0.0185
10	CDI	0.1038	0.0426	0.0317	0.0327	0.0349	0.0323
	HQ	0.0649	0.0266	0.0198	0.0204	0.0218	0.0202
11	CDI	0.0808	0.0331	0.0247	0.0254	0.0272	0.0251
	HQ	0.0505	0.0207	0.0154	0.0159	0.0170	0.0157
12	CDI	0.1391	0.0570	0.0425	0.0438	0.0468	0.0432
	HQ	0.0870	0.0357	0.0266	0.0274	0.0292	0.0270
13	CDI	0.1204	0.0494	0.0368	0.0379	0.0405	0.0374
	HQ	0.0753	0.0309	0.0230	0.0237	0.0253	0.0234
14	CDI	0.0746	0.0306	0.0228	0.0235	0.0251	0.0232
	HQ	0.0466	0.0191	0.0142	0.0147	0.0157	0.0145

But when compared with other parts of the world where they were recording high concentration of nitrate ions in the groundwater basin located Shanmuganadhi River South India, which reached to (160) ppm (Karunanidhi et al, 2019) and (348) ppm in the northeastern part of the Siddipet district of Telangana, South India (Adimalla and Wu, 2019). Ward et al, (2018) Also indicates that the concentration reached 1063 ppm in some parts of Manitoba and Colombia, due to the increase in population and agricultural activities in these regions.

As for the evaluation of groundwater in the Abu Wajnah area in terms of health risks to humans, there are no risks of developing cancerous diseases when using this groundwater for drinking by the residents of the region, due to the low concentrations of nitrate ions much less than the limits allowed (45) ppm by the World Health Organization (WHO, 2017; US. EPA, 2005).

As for Non-cancerous risks, the results of the hazard quotient of nitrates ($HI_{\text{nitrate}} = HQ$) values shown in the table (2) are indicated that the values of HQ for ages less than one year, and ages 6 to 11, 11 to 16, 18 to 21, 18 to 65 and over 65 years ranged between (0.0466 to 0.1125, 0.0191 to 0.0461, 0.0142 to 0.0344, 0.0147 to 0.0354 0.0157 to 0.0378, 0.0145 to 0.0349) respectively, which indicates that there are no health risks because all values of total human health risks (HQ or HI_{nitrate}) were within internationally permissible limits (less than 1) (Adimalla and Wu, 2018).

It is also noted from Table (2) that the values of the chronic daily intake (CDI) and hazard quotient (HQ) or the hazard index resulting from nitrate ion (HI_{nitrate}) and for each water quality was higher for children under one year of age compared to the rest of the studied ages, which reached to (0.1125 and 0.1800) respectively, then the values increase significantly at ages 18 to 65 years compared to the rest of the age groups and this is due to some factors including like exposure duration (ED), body weight (BW) and average time (AT) (Zang et al, 2019).

Thank God, the groundwater in the village of Abu Wajnah does not pose any risk to the health of consumers, including children, when used for drinking in relation to the risks of nitrate ions, both non-cancerous and cancerous risks (He et al, 2018; US. EPA, 2005), while many regions of the world and even the United States of America (USA) suffers from problems of high nitrate concentrations in the groundwater used for drinking, as the Centers for Disease Control and Prevention indicates that there are many deaths of infants due to blue baby syndrome (methemoglobinemia) in Texas, South Dakota and Louisiana, Virginia and Colorado, as well as the Eastern European countries (Knobloch et al., 2000), studies also, conducted in the USA and Denmark indicated an increased risk of developing cancerous diseases when drinking water is contaminated with high levels of nitrates such as colon

and rectal cancer (McElroy et al, 2008; Schullehner et al, 2018)

CONCLUSIONS AND RECOMMENDATIONS

1. The current study is the first of its kind in Iraq that dealt with the Human health risks which (HHR) which depended on the age groups, exposure rate, body weight, daily consumption of drinking water, etc. as well as the concentration of nitrates in water
2. Low levels of nitrate in drinking water sources of the village of Abu committee is far less than the permitted levels globally.
3. Low nitrate risk quotient values ($HI_{\text{nitrate}} = HQ$) for all age groups, especially children below levels that are dangerous to human health. Thus, The studied water sources are healthy and safe to drink about the concentration of nitrate ions and there are no health risks, whether cancerous or non-cancerous.

Therefore, the study recommends the use of studied water for drinking, while raising awareness for well owners by preserving them from pollution sources, and conducting periodic checks for this groundwater to stand in case of any emergency and finally, conducting such a study on water sources in other regions of Iraq.

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REFERENCES

1. Adimalla, N.; Li, P.Y. Occurrence, health risks, and geochemical mechanisms of fluoride and nitrate in groundwater of the rock-dominant semi-arid region, Telangana State, India. *Hum. Ecol. Risk Assess*, 2019; 25: 81–103.
2. Adimalla, N.; Wu, J.H. Groundwater quality and associated health risks in a semi-arid region of south India: Implication to sustainable groundwater management. *Hum. Ecol. Risk Assess*, 2019; 25: 191–216.
3. Ahmed, G., AH Santuraki, A. H. and Mukhtar, M. Assessing the pollution indicator in groundwater in Hadejia metropolis, Jigawa state, Nigeria. *Int. J. of Chemistry Studies*, 2019; 3(2): 11-13.
4. Al-Hamdany, N. A. S., Al-Shaker, Y. M. S. and Al-Saffawi, A. Y. T. Application of nitrate pollution index (NPI) to evaluate the health safety of wells water for some quarters of the left side of Mosul city, Iraq. Accepted for publication in *Biochem. Cell. Arch*, 2020; 02: (Issue 2).
5. Al-Mashhdany, M. H. S., Al-Mamaree, J. A. A. and Al-Saffawi, A. A. Y. T. Valuation of water for

- drinking and domestic purposes using (WQI). Case study: groundwater of Abu-wagnah village, Tal-Afar district. Iraq. accepted for publication in Plant Archives Journal, 2020.
6. Al-Saffawi, A Y T, Ibn Abubakar B SU, Abbass, L Y and Monguno, A.K. Assessment of groundwater quality for potential irrigation purposes using water quality index (IWQI) in Al-Kasik subdistrict, Iraq. Nigerian J. of Eng. Techn. (NIJOTECH), 2020a; 39(2): 632 – 638. <http://dx.doi.org/10.4314/njt.v39i1.35>.
 7. Al-Saffawi, A. Y. T. (2019). Water quality of Nimrud district wells southeast of Mosul city for drinking and civil purpose using the canadian model of water quality. Pak. J. Anal. Environ. Chem, 2019; 20(1): 75 – 81. <http://doi.org/10.21743/pjaec/2019.06.10>.
 8. Al-Shanona, R. A. A., Al-Sardar, N. M. S. and Al-Saffawi, A. Y. T. Water quality assessment for irrigation and livestock drinking in Abu Maria village/ district of Tall-Afar-Iraq. J. of Environmental Studies [JES], 2018; 18: 9-14.
 9. APHA. "Standard method for examination of water and waste water". 23rd ed., Washington, DC, USA. <https://doi.org/10.2105/SMWW.2882.089>, 2017.
 10. Bray, F. et al. Global cancer statistics GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin, 2018; 68: 394–424.
 11. Breda, S. G., Mathijs, K., Kiss, V., Kuhnle, G. G., Veer, B., Jones, R. R., Sinha, R., Ward, M. H. and Kok, T. M. Impact of high drinking water nitrate levels on the endogenous formation of apparent N-nitroso compounds in combination with meat intake in healthy volunteers. Envi. Health, 2019; 18: 87-99. <doi.org/10.1186/s12940-019-0525-z>.
 12. CDC (Centers for Disease Control and Prevention). Spontaneous abortions possibly related to ingestion of nitratecontaminated well water—LaGrange County, Indiana, 1991–1994. MMWR Morb Mortal Wkly Rep, 1996; 45: 569–572.
 13. He, X., Wu, J. and He, S. Hydrochemical characteristics and quality evaluation of groundwater in terms of health risks in Luohe aquifer in Wuqi County of the Chinese Loess Plateau, northwest China. Human and Ecol. Risk Assess. Taylor & Francis Group, LLC. <https://doi.org/10.1080/10807039.2018.1531693>, 2018.
 14. Huana, H., Hu, L., Yang, Y., Jia, Y., Lian, X., Ma, X., Jiang, Y. and Xi, B., 2020.
 15. Groundwater nitrate pollution risk assessment of the groundwater source field based on the integrated numerical simulations in the unsaturated zone and saturated aquifer Environment Int. 137: 1-10. 105532. <doi.org/10.1016/j.envint.2020.105532>.
 16. Jaafer, A J A and Al-Saffawi (2020) Application the logarithmic water quality index (WQI) to evaluate the wells water in Al-Rashidiya area, north Mosul, for drinking and civilian uses. Accepted for publication Plant archives. 20(1 Special issue), 2020.
 17. Juntakut, P., Haacker, E. M., Snow, D .D. and Ray, C. Risk and Cost Assessment of Nitrate Contamination in Domestic Wells. Water, 2020; 12: 428-443. <doi:10.3390/w12020428>.
 18. Karunanidhia, D., Aravinthasamy, P., Subramanib, T., Wuc, J. and Srinivasa-moorthy, K. Potential health risk assessment for fluoride and nitrate contamination in hard rock aquifers of Shanmuganadhi River basin, South India. Human and Ecol. Risk Assess.: An Int. J., 2019; 1-21. <https://doi.org/10.1080/10807039.2019.1568859>
 19. Knobloch, L., Salna, B., Hogan, A., Postle, J. and Anderson, .H. "Blue babies and nitrate contaminated well water. Environ Health Perspect, 2000; 108(7): 675-678. <https://www.researchgate.net/publication/12414965>
 20. Manassaram, D. M., Backer, L. C. and Moll, D. M. A review of nitrates in drinking water: Maternal exposure and adverse reproductive and developmental outcomes Environmental Health Perspectives, 2006; 114(3): 320-327.
 21. McElroy, J. A., Trentham-Dietz, A., Gangnon, R. E., Hampton, J. M., Bersch, A. J., Kanarek, M. S. and Newcomb, P. A. Nitrogen-nitrate exposure from drinking water and colorectal cancer risk for rural women in wisconsin, USA.j. of water and Health, 2007; 6(3): 399- 409. Doi:10.2166/wh.2008.o48.
 22. Parvizishad, M., Dalvand, A., Mahvi, A.H and Goodarzi, F. A Review of adverse effects and benefits of nitrate and nitrite in drinking water and food on human health. Health Scope, 2017; 6(3): 1– 9. <doi: 10.5812/jhealthscope.14164>.
 23. Schullehner, J., Hansen, B., Thygesen, M., Pedersen, C. B. and Sigsgaard, T. Nitrate in drinking water and colorectal cancer risk: A nationwide population-based cohort study. Int. J. Cancer, 2018; 143: 73–79.
 24. Talat R. A., Al-Assaf, A. T. R. and Al-Saffawi, A. Y. T. Valuation of water quality for drinking and domestic purposes using WQI: Acase study for groundwater of Al-Gameaa and Al-Zeraee quarters in Mosul city/Iraq. IOP Conf. Series: Journal of Physics: Conf. Series), 2019; 1-10. <doi:10.1088/1742-6596/1294/7/072011>. U.S.EPA. Guidelines for Carcinogen Risk Assessment. Environmental Protection Agency. Washington, DC. P: 166. www.epa.gov/risk/guidelines-carcinogen-risk, 2005.
 25. Vermeer, I. T. M., Pachen, F. D. M., Dallinga, J. W., Kleinjans, J. C. S. and Maanen, M. S. Volatile N-Nitrosamine Formation after Intake of Nitrate at the ADI Level in Combination with an Amine-rich Diet Environmental Health Perspectives, 1998; 106(8): 459-463.
 26. Ward, M. H., Jones, R. R., Brender, J. D., Kok, T. M., Weyer, P. J., Nolan, B. T., Villanueva, C. M. and Van Breda S. G. Drinking Water Nitrate and Human Health: An Updated Review. Int. J. Environ.

- Res. Public Health, 2018; 15: 1557-1587.
doi:10.3390/ijerph15071557.
27. WHO, idelines for Drinking-water Quality, forth edition. World Health Organization. Switzerland, 2017; 631.
28. Yu, M., Li, C., Hu, C., Jin, J., Qian, S. and Jin, J. The relationship between consumption of nitrite or nitrate and risk of non-Hodgkin lymphoma. Scientific Reports, 2020; 10: 551-560.
doi.org/10.1038/s41598-020-57453-5
29. Zhang, Q., Xu, P. and Qian, H. Assessment of Groundwater Quality and Human Health Risk (HHR) Evaluation of Nitrate in the Central-Western Guanzhong Basin, China. Int. J. Environ. Res. Public Health, 2019; 16: 4246-4262.
doi:10.3390/ijerph16214246.
30. Zuckerbraun, B. S., George, P. and Mark T. Gladwin, M. T. Nitrite in pulmonary arterial hypertension: therapeutic avenues in the setting of dysregulated arginine/nitric oxide synthase signalling. Cardiovascular Res., 2011; 89: 542–552.
doi:10.1093/cvr/cvq370.