

## Infants Methemoglobinemia Due to Nitrate Contaminated in Rural Water Supplies in the Region of Al-Jebel Al-Akhdar-Libya

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**Abstract:** The use of nitrate-contaminated drinking water to prepare infant formula is a well-known risk factor for infant Methemoglobinemia. Affected infants develop a peculiar blue-gray skin colour and may become irritable or lethargic, depending on the severity of their condition. The condition can progress rapidly to cause coma and death if it is not recognized and treated appropriately. Therefore, in this work we decided to study this phenomenon as health problem related directly or indirectly to chemicals water pollution. The results shown increased the Nitrates concentration level in water sources were found in certain area of the study. The highest value of nitrates ( $\text{NO}_3$ ) were observed in the sites of (Al-Haniya and Al-Usita) at values of (52.33 and 51.6 mg/L) respectively, which is higher or close to permissible limits of  $\text{NO}_3$  in drinking water according to Libyan and WHO standards (45 mg/L). Interesting link were obtained in this study indicated a possible correlation between the Methemoglobinemia and the  $\text{NO}_3$  contaminated drinking water in the study area. The results shown that there are no any diagnosed Methemoglobinemia (Confirmed Cases) versus that the results shown that there are 165 (Possible Cases) cyanotic infants undiagnosed (the main symptom of the infants Methemoglobinemia) under 6 months age. So, we can assume that the non-diagnosed infant's cyanosis cases can be Infants Methemoglobinemia disease due to the possibility of  $\text{NO}_3$  contaminated water.

**Key words:** Methemoglobinemia • Nitrates • Undiagnosed disease • Cyanosis • Infant's • Human health

### INTRODUCTION

Information on water quality in relation to human health in the study area of Al-Jabal Al-Akhdar, Libya is sparse and it tends towards the deterioration of the aquifer [1, 2]. Therefore, an existing hydro chemical data in the basins are required in this work to provide strong evidence on nitrate ( $\text{NO}_3$ ) level on water quality in relation to Infants Methemoglobinemia disease.

Nitrate- contaminated well water is a common cause of acquired Methemoglobinemia in rural, formula-fed infants [3]. The disease can be caused by intake of water and vegetables high in nitrate, exposure to chemicals containing  $\text{NO}_3$ , or can even be hereditary. Nitrate itself is not toxic to humans; nitrate becomes a problem only when it is converted to nitrite ( $\text{NO}_2$ ) in the human body, resulting in Methemoglobinemia [4]. Much of the ingested  $\text{NO}_3$  is usually absorbed before reaching the nitrate-

reducing bacteria, which reside in the intestinal tract [5]. Most of the ingested  $\text{NO}_3$  is excreted within 24 hours mainly through urine, as well as through feces and sweat. If nitrate is introduced directly into the colon, Methemoglobinemia is readily produced [3]. Nitrite ( $\text{NO}_2$ ) produced from nitrate ( $\text{NO}_3$ ) enters the bloodstream mainly through the upper gastrointestinal tract [6]. Nitrate is converted to  $\text{NO}_2$  by intestinal bacteria and nitrite acts as the oxidizing agent to form MetHb in the red blood cells [7]. Measurement of Methemoglobin concentrations in blood has been used as a biomarker of effect for infants and children. Some studies found an association between concentrations of Methemoglobin in blood and  $\text{NO}_3$  exposure, but other studies did not [6]. The most common environmental cause of Methemoglobinemia in infants in the United States is ingestion of water contaminated with  $\text{NO}_3$  from agricultural fertilizers, barnyard runoff, or septic-tank effluents [8].

Methemoglobinemia occurs whenever there is excess oxidized hemoglobin and the systems that reduce it to its ferrous state are overwhelmed, impaired, or lacking. The three common causes of Methemoglobinemia are exogenous (toxin-induced), endogenous (related to diarrhoea infection, or systemic acidosis) and genetic [5]. The hallmark sign of Methemoglobinemia is the slate-blue skin color, termed cyanosis, in the presence of a normal partial pressure of arterial oxygen. Other clinical symptoms, including headache, fatigue, dyspnea and lethargy are generally seen only in cases of acquired Methemoglobinemia. Cyanosis becomes apparent when the methemoglobin level exceeds 1.5 g/dl (usually 1-15% total hemoglobin). Blood from an affected patient has a characteristic chocolate-brown appearance that does not change when the sample is exposed to oxygen [3]. It has been demonstrated by [9] that two recent cases of infant Methemoglobinemia, or blue baby syndrome, that were associated with the use of water from shallow private wells contaminated with Nitrates. These cases serve as reminders of the hazard that nitrate-contaminated water poses to infants during the first 6 months of life.

Because there are several cyanotic cases infants that undiagnosed in Al-Jabal Al-Akhdar, Libya (study area), we decided in this work to study this phenomenon as health problem related to drinking water used in this region. Chemical analyses test on drinking water sources in the study area were subjected with particular reference to nitrate-contaminated water. Although the sampling and analytical background on NQ as chemical pollutant in drinking water to these measurements has not been recorded in relation to Methemoglobinemia disease in the study area.

## **MATERIALS AND METHODS**

The number of 22 deep Wells (underground water) were taken and three replicates were made for each of various fields in the study area of Al-Jabal Al-Akhdar region, Libya (2010-2014). The water samples were analyzed at different season (summer and winter). Moreover, the following aspects have been analysed in the study area: Water quality (chemical and physical analyses) and epidemiology of the disease particularly Methemoglobinemia in infants under 6 months of age.

Analytical work in this study were carried out by the qualified and technical's laboratory staff at Faculty of Natural Resources, University of Omar Al-Mukhtar, Al-Baida Libya, and the support of the medical qualified

staff at Medicine & surgery Faculty, Politecnecadelle Marche University, Italy. All the methods used of the study were the most up-to-date available in the above universities to draw attention on water pollution problem effects on human health as affected by climatic changes and human activities.

Thus a survey of this pollution sources was carried out by a wide range of chemical and physical parameters on water including ; Temp, TDS, EC, pH, DO, ALK, TH, Ca.H, Mg.H, Cl, SO<sub>4</sub>, NO<sub>3</sub>, NO<sub>2</sub>, NH<sub>4</sub>, P, Ca, Mg, Na, K and some heavy metals.

For the method of collection of samples, protection, calibration and chemical analyses see the Environmental Protection Agency [6] and the Standard Method for Examination of Water [10]. Procedures for onsite measurements and for collecting, treating and transferring samples were consistent with ASTM standards (American Society for Testing and Materials).

The current study performed an importance analysis in order to investigate the predictive relationship between the percentages of NO<sub>3</sub> in the water as described in this study in relation to human health as affected by Methemoglobinemia disease. So it was searched in this study for the Cyanosis at infants less than 6 months age, in the Statistics and Documentation Department at the Hospital of Al-Baida city Libya (Mean hospital in the study area).

Personal interviews with Pediatricians that have at least 10 years' experience working at hospitals in the study area were also investigated in this work to know about the Infants Methemoglobinemia disease in the study area.

## **RESULTS**

Water analyses of the study area revealed that there are a natural changes up to moderate ranges of all mentioned ions as shown in the results (Tables 1 and 3). Therefore, with exception of NO<sub>3</sub> in certain sites of the study area (Table 1), from all sites examined in this work were generally acceptable for human consumption and domestic use according to international (WHO) standards [11].

There is a significant difference between areas in the NO<sub>3</sub> concentration level in water, where the highest value obtained in the winter was (52.33 mg/L and 51.6 mg/L) in the Al Haniya and Al-Uisit sites respectively, this value highest than the acceptable standards of Libyan and WHO (45 mg/L), the lower value was (10.2 mg/L) in the Samalossite.

Table 1: Water chemical parameters test (mg/L) for summer season.

No	Sites	Temp	pH	DO	EC	TDS	NO <sub>3</sub>	NO <sub>2</sub>	Phosphate	Calcium	Chloride
1	Massah	21.6	6.99	7.2	1135	681	22.80	0.03	0.40	75.3	78.3
2	Omar Al-Mukhtar	23.8	7.17	6.5	1184	705	14.20	0.02	0.29	66.1	81.1
3	Marawah	21.8	7.32	5.1	1250	800	10.40	0.02	0.11	85.0	65.3
4	Qaser Libya	19.9	7.20	6.2	1122	798	19.32	0.10	0.13	70.1	76.3
5	Al-Hamamah	23.6	7.20	5.6	1109	650	19.52	0.02	0.38	70.0	74.7
6	Al-Haniya	24.0	6.96	8.2	1320	1000	29.65	0.10	0.53	80.0	110
7	Al-Ucita	23.1	7.20	7.9	1378	1067	28.85	0.89	0.47	84.1	98.7
8	Zawit Al-Argub	20.2	7.00	7.1	1330	695	19.11	0.24	0.45	79.2	99.1
9	Eqfenta	20.1	6.82	6.9	1328	754	25.10	0.15	0.51	69.2	78.2
10	SediAbdalwahed	21.2	7.20	6.2	1298	712	16.22	0.13	0.42	64.1	76.4
11	Al-Bayda	24.7	7.14	5.4	1211	695	11.70	0.07	0.52	71.7	79.9
12	Suluntah	24.1	7.00	5.6	1296	758	14.67	0.25	0.27	60.6	74.4
13	Qandulah	23.2	6.99	4.4	1216	698	19.12	0.05	0.52	74.4	80.3
14	Gardas Al Giarari	23.5	6.89	5.6	1082	645	15.80	0.04	0.18	63.4	75.1
15	Samalos	24.4	7.10	5.8	1063	693	21.60	0.03	0.30	69.7	81.6
16	Al Kwaymat	24.4	7.11	6.6	1234	712	20.16	0.21	0.22	81.1	98.2
17	Sussah	23.9	7.59	5.5	1203	721	12.50	0.06	0.61	77.2	82.9
18	Shahat	21.0	7.45	6.3	1303	752	35.14	0.07	0.82	78.5	86.5
19	LabraqDabossia	20.0	7.07	7.4	1127	664	16.20	0.02	0.47	73.0	76.3
20	Qernadah	23.6	7.18	5.2	1044	589	16.20	0.05	0.06	69.1	67.1
21	Faydiyah	20.6	6.61	4.9	1071	599	17.10	0.04	0.13	59.0	79.0
22	Al-Qyqab	22.4	7.16	5.3	1077	579	11.00	0.04	0.72	66.1	66.5

Continued

Table 1: Water chemical parameters test (mg/L) for summer season.

No	Sites	Sulphate	Magnesium	Sodium	Potassium	Alkalinity	Hardness	Iron	Copper	Zinc	lead	Cadmium
1	Massah	50.18	20.56	45.63	6.79	322	272	0.002	0.005	0.002	0.001	0.001
2	Omar Al-Mukhtar	50.72	18.14	47.24	1.90	286	240	0.004	0.003	0.002	0.003	0.002
3	Marawah	44.45	59.00	73.00	4.10	164	455	0.003	0.006	0.002	0.005	0.004
4	Qaser Libya	46.12	49.32	53.41	4.87	312	341	0.002	0.004	0.003	0.004	0.001
5	Al-Hamamah	48.1	19.2	43.50	2.70	291	254	0.004	0.004	0.002	0.004	0.002
6	Al-Haniya	54.32	79.00	65.00	2.45	228	384	0.004	0.003	0.005	0.003	0.004
7	Al-Ucita	57.44	58.32	62.77	5.34	209	351	0.005	0.004	0.004	0.004	0.003
8	Zawit Al-Argub	51.11	60.14	48.66	3.66	223	245	0.004	0.002	0.003	0.004	0.001
9	Eqfenta	46.34	52.34	53.37	3.78	265	218	0.004	0.002	0.003	0.003	0.001
10	SediAbdalwahed	49.16	49.65	53.12	2.54	189	203	0.003	0.002	0.002	0.003	0.001
11	Al-Bayda	51.84	19.65	46.56	1.10	310	260	0.005	0.004	0.003	0.003	0.001
12	Suluntah	55.52	16.62	50.78	1.10	270	220	0.004	0.005	0.003	0.005	0.001
13	Qandulah	51.65	20.41	46.77	2.10	298	270	0.004	0.005	0.005	0.005	0.003
14	Gardas Al Giarari	50.64	17.38	43.75	1.80	276	240	0.004	0.003	0.006	0.004	0.002
15	Samalos	48.98	36.79	47.2	6.64	312	283	0.001	0.003	0.001	0.001	0.001
16	Al Kwaymat	54.23	59.34	56.33	5.18	132	287	0.005	0.001	0.003	0.005	0.001
17	Sussah	44.16	21.16	48.31	2.52	291	280	0.002	0.005	0.002	0.005	0.004
18	Shahat	55.6	21.53	50.38	5.37	320	285	0.002	0.002	0.002	0.001	0.001
19	LabraqDabossia	49.14	19.90	44.48	1.80	315	265	0.005	0.004	0.004	0.001	0.001
20	Qernadah	47.67	19.20	40.33	2.70	279	269	0.002	0.005	0.002	0.001	0.004
21	Faydiyah	45.66	37.00	36.00	1.61	172	248	0.003	0.003	0.005	0.001	0.002
22	Al-Qyqab	53.64	18.13	38.79	1.80	289	240	0.003	0.006	0.002	0.004	0.004

Table 2: Water chemical parameters test (mg/L) for winter season

No	Sites	Temp	pH	DO	EC	TDS	NO <sub>3</sub>	NO <sub>2</sub>	Phosphate	Calcium	Chloride
1	Massah	18.2	7.35	5.3	1611	956	49.00	1.61	0.61	89.57	104.0
2	Omar Al-Mukhtar	16.2	7.22	8.9	1520	875	33.60	0.18	0.83	74.85	93.45
3	Marawah	17.4	7.25	6.7	1260	810	10.50	0.04	0.10	90.00	72.14
4	Qaser Libya	16.7	7.30	8.8	1346	824	23.70	0.10	0.65	67.93	84.13
5	Al-Hamamah	18.0	7.26	8.6	1589	819	38.89	0.22	0.54	90.02	163.0
6	Al-Haniya	17.3	6.77	9.7	1630	1100	52.33	1.30	0.82	89.00	177.0
7	Al-Ucita	17.8	7.10	9.8	1614	1136	51.60	1.14	0.89	85.14	187.0
8	Zawit Al-Argub	15.5	6.80	8.2	1560	812	24.20	0.12	0.73	84.55	165.0
9	Eqfenta	15.8	6.72	8.3	1583	813	34.50	0.19	0.65	87.23	94.72
10	SediAbdalwahed	16.3	7.11	7.9	1566	820	17.80	0.08	0.59	69.79	91.98
11	Al-Bayda	14.2	7.34	7.3	1341	782	30.00	0.13	0.47	79.37	81.88
12	Suluntah	14.7	7.38	7.7	1216	791	31.67	0.16	0.36	80.12	75.81
13	Qandulah	14.4	7.54	5.6	1239	788	39.58	0.29	0.34	77.39	79.13
14	Gardas Al Giarari	14.2	7.38	5.2	1211	801	24.60	0.12	0.27	75.63	84.22
15	Samalos	18.3	6.65	5.9	1275	791	10.20	0.01	0.33	79.87	69.55
16	Al Kwaymat	18.3	6.70	6.1	1282	774	10.60	0.01	0.29	80.20	72.77
17	Sussah	18.6	7.10	8.5	1358	828	22.00	0.01	0.31	80.35	73.45
18	Shahat	12.3	8.00	8.4	1516	873	38.00	0.21	0.25	85.71	88.89
19	LabraqDabossia	17.8	7.38	8.0	1326	788	16.72	0.06	0.23	78.82	87.17
20	Qernadah	15.4	6.90	8.2	1251	700	17.77	0.08	0.74	77.76	76.10
21	Faydiyah	17.9	7.42	6.2	1185	610	18.77	0.05	0.15	70.00	97.00
22	Al-Qyqab	14.3	7.12	6.8	1212	645	19.45	0.05	0.13	78.94	78.16

Continued

Table 2: Water chemical parameters test (mg/L) for winter season.

No Sites		Sulphate	Magnesium	Sodium	Potassium	Alkalinity	Hardness	Iron	Copper	Zinc	lead	Cadmium
1	Massah	67.0	24.6	60.7	7.37	370	325	0.008	0.004	0.009	0.001	0.001
2	Omar Al-Mukhtar76.1	53.2	66.5	6.90	365	367	0.007	0.004	0.009	0.001	0.001	
3	Marawah	51.1	54.0	70.0	4.72	189	447	0.003	0.004	0.003	0.009	0.001
4	Qaser Libya	65.3	52.6	69.4	5.10	342	406	0.003	0.0041	0.003	0.008	0.001
5	Al-Hamamah	75.1	84.1	70.3	4.43	298	432	0.007	0.003	0.007	0.007	0.001
6	Al-Haniya	61.2	87.0	87.0	5.20	247	489	0.008	0.005	0.006	0.006	0.004
7	Al-Usita	62.3	73.0	86.3	4.12	267	453	0.007	0.004	0.005	0.005	0.003
8	Zawit Al-Argub	67.2	74.6	78.4	3.89	302	312	0.008	0.004	0.004	0.005	0.001
9	Eqfenta	54.8	69.5	75.5	4.13	312	310	0.006	0.004	0.005	0.007	0.001
10	SediAbdalwahed	56.6	67.4	57.3	3.96	269	298	0.005	0.004	0.004	0.006	0.001
11	Al-Bayda	52.7	21.7	47.7	3.00	305	288	0.004	0.004	0.003	0.003	0.009
12	Suluntah	58.1	34.3	46.1	3.43	286	278	0.005	0.003	0.003	0.002	0.006
13	Qandulah	49.2	31.2	43.6	3.22	313	266	0.006	0.004	0.003	0.004	0.003
14	Gardas Al Giarari	53.4	24.1	51.2	2.89	291	291	0.005	0.004	0.002	0.004	0.001
15	Samalos	54.6	27.3	53.4	2.79	305	321	0.006	0.003	0.009	0.003	0.003
16	Al Kwaymat	56.7	21.5	46.3	3.24	289	302	0.006	0.004	0.003	0.004	0.001
17	Sussah	61.2	22.5	54.3	3.12	306	285	0.007	0.003	0.004	0.003	0.001
18	Shahat	57.2	23.5	51.8	6.53	345	300	0.026	0.005	0.009	0.001	0.001
19	LabraqDabossia	56.1	21.6	50.7	2.10	330	286	0.007	0.006	0.001	0.001	0.001
20	Qernadah	54.6	21.1	47.9	3.78	300	305	0.002	0.005	0.009	0.003	0.003
21	Faydiyah	50.1	36.0	48.0	1.84	197	276	0.003	0.003	0.003	0.004	0.001
22	Al-Qyqab	51.3	34.2	50.5	2.11	198	291	0.003	0.003	0.003	0.003	0.001

Table 3: Summary of the study results.

No	Sites	Populations (Thousands)	Cyanosis Cases			Cyanosis Cases %			Dead with Cyanosis	Morbidity /1000	Mortality /1000	Nitrate (mg/L)	Nitrite (mg/L)	Coordinates		
			Newborn	2010	2011	2012	2010	2011						2012	Latitude	Longitude
1	Massah	29919	749	7	11	18	0.93	1.46	2.40	0	48.06	0	49.0	1.61	32.751676	21.626377
2	Omar Al-Mukhtar	10519	264	1	3	5	0.37	1.13	1.89	0	34.10	0	33.6	0.18	32.630606	21.675003
3	Marawah	7806	196	0	1	2	0	0.51	1.02	0	15.31	0	10.5	0.04	32.486415	21.408626
4	Qaser Libya	9593	240	0	0	3	0	0	1.25	0	12.50	0	23.7	0.10	32.614516	21.399925
5	Al-Hamamah	1760	44	0	0	1	0	0	2.27	0	22.72	0	38.9	0.22	32.914445	21.628773
6	Al-Haniya	7504	188	0	1	0	0	0.53	0	0	5.32	0	52.3	1.30	32.841102	21.520844
7	Al-Usita	916	23	0	1	1	0	4.34	4.34	0	86.95	0	51.6	1.14	32.875631	21.661804
8	Zawit Al-Argub	5183	130	0	0	1	0	0	0.76	0	7.69	0	24.2	0.12	32.665443	21.543956
9	Eqfenta	1000	25	0	1	0	0	4	0	0	40.0	0	34.5	0.19	32.732671	21.588424
10	SediAbdalwahed	1865	47	0	0	0	0	0	0	0	0.00	0	17.8	0.08	32.726221	21.579572
11	Al-Bayda	169738	4252	10	22	32	0.23	0.51	0.75	6	15.05	1.41	30.0	0.13	32.765892	21.743339
12	Suluntah	11550	289	1	1	3	0.34	0.34	1.03	1	17.30	3.46	31.7	0.16	32.590175	21.715807
13	Qandulah	4913	123	0	0	0	0	0	0	0	0	0	39.6	0.29	32.538108	21.577185
14	Gardas Al Giarari	821	21	0	0	0	0	0	0	0	0	0	24.6	0.12	32.528312	21.786656
15	Samalos	437	11	0	0	0	0	0	0	0	0	0	10.2	0.01	32.205534	21.863552
16	Al Kwaymat	897	22	0	0	0	0	0	0	0	0	0	10.6	0.01	31.947137	21.863552
17	Sussah	8987	225	0	1	1	0	0.44	0.44	0	8.89	0	22.0	0.01	32.897487	21.967408
18	Shahat	31308	784	3	4	8	0.38	0.51	1.02	3	19.13	3.83	38.0	0.21	32.807769	21.869374
19	Labraq	9226	231	0	1	2	0	0.43	0.86	1	12.99	4.33	16.7	0.06	32.788611	22.000074
20	Qernadah	2058	52	1	1	2	1.92	1.92	3.84	0	76.92	0	17.8	0.08	32.731902	21.903821
21	Faydiyah	9092	228	1	1	4	0.43	0.43	1.75	2	26.31	8.77	18.7	0.06	32.688086	21.906165
22	Al-Qyqab	10000	251	2	3	4	0.79	1.19	1.59	0	35.86	0	19.4	0.05	32.730515	22.007391
Total		335092	8395	26	52	87				13						

In addition water analyses showed high EC and TDS values (Electrical Conductivity and Total Dissolved Salts) in the most examined waters in the study area reaching (1630 and 1614 ms/cm<sup>-1</sup>/25 °C) that led to higher value of TDS (1100 and 1136 mg/L) at Al Haniya and Al-Usita region respectively. However, this high values of EC and TDS is presumably masked by the much greater influence of chloride (Cl<sup>-</sup>) and NO<sub>3</sub> as found in this study (Table 1 and 2).

Moreover, results (Table 1) showed the presence of dissolved oxygen (DO) were found in some area of the study. Noted that the highest percentage of dissolved oxygen on water were recorded at Al-Usita site in the

winter season at value (9.8 mg/L) and the lower value was found at Gardas Al-Giarari site at value (5 mg/L). Similar trends of dissolved oxygen (DO) in water were also found in summer season, but with less value at Al-Haniya site at value (8.2 mg/L) whereas the lowest values recorded in the Qandulah site where was (4.4 mg/L). The presence of dissolved oxygen in the water as found in the study (Table 1) might leads to an anaerobic analysis of pollutants produced on it the presence of harmful gases in the water as well as reductase of nitrate to nitrite.

A conducted survey study (Questionnaire) and personal interviews with 53 Pediatricians that have at least 10 years' experience, about the Infants

Methemoglobinemia disease in the study area, reported that they did not diagnosing any case throughout the period of their work, and 84.90% of them answered about the reason, that the disease is rare, 62.26% reported that there is no any consideration or importance for this disease in the study area.

Moreover, questionnaire results conclude that there are not any diagnosed Methemoglobinemia (Confirmed Cases). While the medical patients' files at the main Hospital in the study area reported that there are 165 (Possible Cases) cyanotic infants undiagnosed (Methemoglobinemia) included 13 deaths of infants under 6 months (Table 3).

### **DISCUSSION**

The case diagnosis (confirmed case) has included infants less than 6 months of age hospitalised with signs and symptoms of Methemoglobinemia during the period of study. In order to increase the sensitivity of the case ascertainment, a possible case of Methemoglobinemia has been introduced and defined by the medical records available for cyanosis the major symptoms of this disease.

So it was searched the patients' files at the main hospital in the study area at Biedacity for the cyanosis for infants less than (6) months. Note that the cyanosis is not considered of the main symptoms only for the Methemoglobinemia disease but is found in many other diseases such as congenital heart defects, severe flu, whooping cough, bronchiolitis and other.

Although, the medical files conclude that there are not any diagnosed Methemoglobinemia (Confirmed Cases), versus that some files shown that there are 165 (Possible Cases) cyanotic infants undiagnosed (infants Methemoglobinemia) included 13 deaths of infants under 6 months (Table 4).

In addition, a conducted survey study (Questionnaire) and personal interviews with 53 Pediatricians that have at least 10 years' experience, about the Infants Methemoglobinemia disease were concluded in this study. The participation rate to all questions was 90.42%, where their opinions were 96.22% reported that they did not diagnosing any case of infants Methemoglobinemia throughout the period of their work and 84.90% of them answered about the reason, that the disease is rare, 62.26% reported that there is no any consideration or importance for this disease (at medical conferences, scientific research, etc.). Others 79.24% reported that diagnostic services are unavailable like

specialist technical laboratory service. They confirm that some cases of within its symptoms the cyanosis have transferred them to an advanced hospitals at different region of the country. However, the infants Methemoglobinemia disease can be caused by intake of water containing  $\text{NO}_3$ , or can even be hereditary.

In addition, families with private water supplies should conduct annual or semi-annual testing and avoid drinking the water if the nitrate-N concentration exceeds the federal drinking water standard of 10 mg/L [9]. Infants under 6 months of age are particularly susceptible to Methemoglobinemia because they have lower amounts of a key enzyme, NADH-cytochrome b5 reductase (Methemoglobin reductase), which converts methemoglobin back to hemoglobin. Infants begin making adult levels of this enzyme by about 6 months of age [12]. Measurement of methemoglobin concentrations in blood has been used as a biomarker of effect for infants and children. Some studies found an association between concentrations of methemoglobin in blood and nitrate exposure, but other studies did not [6].

Although Methemoglobinemia may be confused with cyanotic congenital heart defects, the cyanosis of infants with congenital heart defects usually improves at least somewhat with administration of supplemental oxygen. Signs and symptoms of Methemoglobinemia vary, depending on the percentage of methemoglobin. Methemoglobinemia results when the amounts of methemoglobin in the blood become high enough to manifest clinical symptoms of cyanosis, usually about 15% of total circulating hemoglobin [7].

In this work, according to what showing to us from the results of tests drinking water in the study area, which showed the existence of evidence of  $\text{NO}_3$  contamination in certain sites of the region (Tables 1 and 2), noting that all of the factors that help the high level of  $\text{NO}_3$  in drinking water are available in the study area such as (overuse of fertilizers, chemicals, leak wastewater to the aquifer). Results indicated the highest concentration of  $\text{NO}_3$  were found at Al-Haniya site particularly in winter season at level (52.33 mg/L). This result is higher than the standard levels of Libya and the World Health Organization (WHO) for drinking water (45 mg/L) [11]. Similarly, at Al-Usita site in the study area the concentration of  $\text{NO}_3$  was found as 51.6 mg/L which are higher than the standards levels of Libya and the World Health Organization for drinking water. Those above two sites are of the most important agricultural areas in the region, are famous with its abundance of agricultural crops.

The high concentration of NO<sub>3</sub> (Table 1 and 2) may relate to some extent of microbiological factors (*E. coli*) as found in certain area due to sewage pollution or agricultural activity (Fertilizers application). This factor can play an important role in making water not suitable for human use (drinking water) [13, 14]. Moreover, the presence of dissolved oxygen in water as found in the study area (Tables 1 and 2) might leads to an anaerobic analyses of pollutants produced on it the presence of harmful gases in the water as well as reductase of NO<sub>3</sub> to NO<sub>2</sub>.

So, we can assume that the undiagnosed infant's cyanosis cases can be Infants Methemoglobinemia disease due to NO<sub>3</sub> contaminated drinking water as found in the study (Tables 1 and 3). These hypotheses are in agreement with many previous studies as described above. Therefore all prenatal and well infant visits to hospitals should include questions about the home water supply. If the source is a private well, the water should be tested for NO<sub>3</sub> level. The NO<sub>3</sub> nitrogen concentration of the water should be <10 ppm. Infants fed commercially prepared infant foods generally are not at risk of nitrate poisoning.

However, home-prepared infant foods from vegetables (eg, spinach, beets, green beans, squash, carrots) should be avoided until infants are three months or older, although there is no any nutritional indication to add complementary foods to the diet of the healthy term infant before 4 months of age. Breastfed are much suitable foods for infants and are not at risk of NO<sub>3</sub> poisoning from mothers who ingest water with high nitrate content (Up to 100 ppm NO<sub>3</sub>), because NO<sub>3</sub> concentration does not increase significantly in the milk [15].

Overall, the findings are the first study on this topic in the country (Libya), which is interestingly consistent with the previous researches in different environments and societies.

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