In: Arsenic
Editor: Andrea Masotti
ISBN: 978-1-62081-320-1

Chapter 8

ARSENIC IN DRINKING WATER AND PREGNANCY OUTCOMES: AN OVERVIEW OF THE HUNGARIAN FINDINGS (1985-2005)

Peter Rudnai, Mihály Csanády, Mátyás Borsányi and Mihály Kádár
National Institute of Environmental Health,
Budapest, Hungary

ABSTRACT

In 1981 a country-wide survey revealed that in South-East Hungary more than 400,000 people were exposed to high levels (> 50 μg/L) of arsenic in the drinking water supplied by certain deep wells. This chapter presents detailed data of three retrospective ecological epidemiological studies conducted between 1985 and 2005 on pregnancy outcomes in the affected area. These studies used district nurses' yearly reports based on the records of pregnancy care units and revealed significant associations between high arsenic levels of the supplied drinking water and the frequency of adverse pregnancy outcomes (stillbirth, perinatal mortality and, especially, spontaneous abortion). As the arsenic level was gradually lowered, the frequency of these adverse birth outcomes also decreased. Significantly increased risk for spontaneous abortions could be observed only in settlements supplied with drinking water containing arsenic above 20 μg/L.

INTRODUCTION

In the southern part of Hungary deep well water has been used for drinking for a long time. In 1981 it was discovered that a considerable part of these deep wells contained arsenic of geological origin. A series of studies revealed that more than 400,000 people living in this area consumed drinking water containing arsenic higher than the health limit value of that time (50 μg/L): the values ranged up to 330 μg/L. The most affected area was Bekes county where 33 settlements were supplied with drinking water exceeding 50 μg/L arsenic level. A

study was initiated to look for health consequences of the arsenic contamination by using available health statistics and registries. (Rudnai and Deák, 1988) Apart from an increased lung cancer mortality rate among the female population of Bekes county, the only apparent sign of the health impact was a statistically significant increase in the incidence of spontaneous abortions and stillbirths in settlements supplied with drinking water above 100 μg/L. The results of this epidemiological study significantly contributed to the decision so that an intervention programme was launched which included establishment of new water works, transportation of water from farther districts or various procedures of arsenic removal. As a result of the intervention arsenic concentration in most settlements was lowered to below 50 μg/L by 2000. However, the World Health Organization and the European Union established a new limit value of 10 μg/L arsenic in drinking water, which was also implemented by the Hungarian law in 2001. Management of a reduction of this size has an enormous financial burden on both the municipalities and the inhabitants, even if state and EU money are also involved. (Implementation of drinking water quality improvement programmes is still in progress in 2012).

Some non-health specialists even claimed that higher arsenic level in drinking water could be allowed in Hungary, because here much less arsenic is consumed with food than in countries surrounded by sea (e.g. Taiwan), from where the epidemiological findings were taken as a basis of the establishment of the new health limit value.

Between 1985 and 2005, three retrospective ecological epidemiological studies were conducted on pregnancy outcomes in the affected area using district nurses' yearly reports based on the records of pregnancy care units. These were the best available sources of health statistics in the area. These studies revealed significant associations between the arsenic level of the supplied drinking water and the frequency of adverse pregnancy outcomes. As the arsenic level was gradually lowered, the frequency of these adverse birth outcomes also decreased.

By the end of 1990-ies the arsenic level in drinking water was below 50 μg/L in most settlements of Hungary. After the new health limit value of 10 μg/L was introduced it was important to see what kind of health effects could be observed in the range between 10 and 50 μg/L arsenic levels. Therefore we conducted a retrospective ecological study on the association between the incidence of adverse pregnancy outcomes and the arsenic level of drinking water in all the 71 settlements of the most affected county (Bekes). Significant increase of risk for spontaneous abortions was found only above 20 μg/L arsenic level of the supplied drinking water and no similar association was observed related to the incidence of stillbirths.

DETAILS OF THE STUDIES

Study 1 (Partly Published in Börzsönyi et al., 1992)

Methods

In the first series of arsenic measurements carried out in 1982-83, a semi-quantitative (Gutzeit method) method was used in settlements where the expected concentration was in line with the aim to be able to detect one tenth (5 μg/L) of the limit value of that time. Where

the arsenic concentration was found about 25 μg/L or higher, the concentration value was verified using photometric method with silverdithiocarbamate; hydride generation or electrothermal atomic absorption methods.

7 villages supplied with drinking water >100 μg/L arsenic level were selected as exposed settlements and 6 villages with drinking water <10 μg/L arsenic served as control ones. Town Bekes with its 22,000 inhabitants was considered an exposed settlement, too (Table 1.)

Pregnancy outcomes were evaluated on settlement level using district nurses' yearly reports since 1970, based on the records of pregnancy care units. The first ecological epidemiological analysis covered only the periods before any intervention in the water supply took place.

Results

The frequency and relative risks of spontaneous abortions and stillbirths in the studied settlements are shown in Table 2. There was significantly higher incidence of both pregnancy outcomes in the exposed settlements. There was no difference in the frequency between the exposed villages and the exposed town Bekes.

Study 2. (Published in Hugarian: Gulyas and Rudnai, 1997)

Before 1984 the arsenic content of the supplied drinking water in town Karcag, a town on the great plain of Hungary with 24,000 inhabitants was between 95 and 130μg/L, i.e. well over the hygienic limit value of 50 μg/L. Due to various interventions the arsenic content started to decrease from 1984 but a steady concentration below 50 μg/L could be reached only from 1990 on. In order to study the adverse effects of drinking water related arsenic exposure, some demographic data for years 1975-95 of Karcag were compared to those of Törökszentmiklós, a town with similar number of inhabitants and to the average values of County Jász-Nagykun-Szolnok. (Table 3.) Before 1984 the frequencies of spontaneous abortion, stillbirth, preterm birth, perinatal and infant mortality were all significantly higher in Karcag than in the reference populations.

From 1984 on, all the mentioned frequencies started to decrease and the difference between the data of Karcag and the whole county, especially in the case of stillbirth and perinatal mortality, became significantly smaller. Between 1990-95, when the arsenic level in the drinking water was steadily below the limit value, the frequencies of spontaneous abortion, stillbirth and perinatal mortality were lower than those in the control town although still slightly higher than the county values.

The relative risks of adverse pregnancy outcomes in the exposed town Karcag for the period between 1975-83 compared to the control town, Törökszentmiklós, and compared to the 1990-95 period of Karcag (after the remediation process) show that the high frequency of spontaneous abortion, stillbirth and perinatal mortality found in Karcag before 1984 may have been related to the high level of arsenic in the drinking water. (Table 4.) The statistical data also reflect the favourable trends, which may be explained by the effectiveness of interventions carried out since 1984 and especially since 1989-90.

Table 1. Characteristics of the study areas

EXPOSED SETTLEMENTS	Inhabitants (01.01. 1984)	As (ug/L) Before intervention	Year of intervention	As (ug/L) After intervention
BUCSA	2,580	100 – 261	1986	22 - 54
ECSEGFALVA	1,756	144 – 270	1991	22 - 48
KÖTEGYÁN	1,637	87 – 209	1990	2 - 22
TARHOS	1,243	92 – 210	1991	4 - 19
TELEKGERENDÁS	1,568	90 – 132	1991	7 - 20
FÜZESGYARMAT	6,337	64 – 112	1994	16 - 21
SZEGHALOM	10,527	60 – 190	1994	15 - 28
Together	25,648			
BÉKÉS (TOWN)	22,289	80 – 270	1987	1 - 45
CONTROL SETTLEMENTS	Inhabitants	(ug/L)		
MEZÔKOVÁCSHÁZA	7,123	Mean: 2.0 (0.0 - 10.0)		
VÉGEGYHÁZA	1,927	Mean: 2.0 (0.0 - 10.0)		
MEZÔHEGYES	7,385	Mean: 3.0 (0.0 - 17.0)		
DOMBEGYHÁZA	2,748	< 10.0		
HUNYA	917	< 10.0		
ÖRMÉNYKÚT	736	< 10.0		
Together	20,836			

Table 2. Relative risks of spontaneous abortions (SpAB) and stillbirths (SB) in settlements exposed to drinking water with arsenic level above 100 µg/L (1970-94)

	Number of live births	Incidence of SpAB (per 1000 live births)	Spontaneous abortions RR (95% C.I.)	Incidence of SB (per 1000 live births)	Stillbirths RR (95% C.I.)
Control villages	6519	42.9		3.23	
Exposed villages	9622	63.3	1.45 (1.26 – 1.66)	7.52	2.32 (1.43 - 3.81)
Town Békés	7786	65.5	1.49 (1.29 – 1.72)	7.71	2.38 (1.47 - 3.84)

Table 3. Demographic data of Karcag (exposed) and Törökszentmiklós (control) in relation to the quality of drinking water

DEMOGRAPHIC PARAMETERS	Karcag			Törökszentmiklós			County Jász-Nagykun-Szolnok		
	1975-83	1984-89	1990-95	1975-83	1984-89	1990-95	1975-83	1984-89	1990-95
Total number of live births	3 910	2 082	1 950	3 663	1 919	1 837	63 206	33 295	31 315
Total number of spontaneous abortions	245	123	90	159	120	99	No data available		
Number of spontaneous abortion per 1000 live births	62,7	59,1	46,2	43,4	62,5	53,9	No data available		
Total number of preterm births	523	241	218	330	174	156	6 601	3 307	2 749
Frequency of preterm births (%)	13,38	11,58	11,18	9,01	9,07	8,47	10,44	9,93	8,78
Total number of stillbirths	48	17	8	28	18	15	630	239	116

DEMOGRAPHIC PARAMETERS	Karcag			Törökszentmiklós			County Jász-Nagykun-Szolnok		
	1975-83	1984-89	1990-95		1975-83	1984-89	1990-95		1975-83
Number of stillbirths per 1000 live births	12,3	8,2	4,1	7,6	9,4	8,2	10,0	7,2	3,7
Total number of perinatal death cases	118	46	30	63	37	35	1 489	590	362
Perinatal mortality (per one thousand)	29,8	21,9	15,3	17,1	19,1	18,9	23,3	17,6	11,5
Total number of infant death cases	111	50	33	74	33	31	1 350	553	401
Infant mortality (per one thousand)	28,4	24,0	16,9	20,2	17,2	16,9	21,4	16,6	12,8

Table 4. Relative risks of adverse pregnancy outcomes of the high arsenic content of the drinking water in Karcag between 1975-83

	Compared to Törökszentmiklós (1975-83) RR (95% C.I.)	Compared to Karcag (1990-95) RR (95% C.I.)
Spontaneous abortions	1.42 (1.17 – 1.72)	1.36 (1.07 – 1.78)
Stillbirths	1.60 (1.01 – 2.54)	2.96 (1.40 – 6.25)
Preterm births	1.48 (1.30 – 1.69)	1.20 (1.03 – 1.39)
Perinatal mortality	1.75 (1.30 – 2.37)	1.96 (1.32 – 2.92)
Infant mortality	1.41 (1.05 – 1.88)	1.68 (1.14 – 2.46)

Study 3. (Published as an Abstract by Rudnai et al., 2006)

Methods

The official definitions of spontaneous abortion and stillbirth were changed from January 1st 1998 (Table 5.), so we could not continue to follow up further changes of these indices. Therefore we started to collect these data according to the new criteria and evaluated the situation in county Bekes.

Table 5. Criteria of spontaneous abortion and stillbirth in Hungary

	Spontaneous abortion		Stillbirth	
	up to 1997	from 1998	up to 1997	from 1998
Time spent in utero	< 28 weeks	< 24 weeks	>28 weeks	> 24 weeks
Body weight	< 1000 g	< 500 g	> 1000 g	> 500 g
Body length	< 35 cm	< 30 cm	> 35 cm	> 30 cm
Sign of life	-	-	No	No
When multiple birth	-	-	At least 1 live foetus	

Data on pregnancy outcomes between 1998 and 2002 were collected for all the 71 settlements of County Bekes, using the annual reports of the district nurses providing pregnancy care for newly registered pregnant women.

Data on the arsenic level of drinking water supplying the settlements were based on the measurements performed in 1999 as part of the National Environmental Health Action Programme. (No changes were recorded in the arsenic levels in these settlements between 1998 and 2002. The new legislation with the 10 μg/L health limit value appeared in 2001.) Poisson regression was used for analysis, using STATA 7.0 programme.

Results

In the 71 settlements during the 5-year period altogether 17,813 live births, 1,062 spontaneous abortions and 135 stillbirths were recorded. (Table 6)

Table 6. Demographic data of County Bekes between 1998-2002

Number of settlements	71
Number of live newborns	17,813
Number (and frequency) of spontaneous abortions	1,062 (5.96%)
Number (and frequency) of stillbirths	135 (7.58 per 1 thousand)

Rates of both spontaneous abortion and stillbirth changed with settlement size: stillbirth rate decreased and spontaneous abortion rate increased with increasing number of population. (Table 7)

Table 7. Pregnancy outcomes according to settlements size

Population	Settlements	Live births	Stillbirths	Stillbirth rate (per 1 thousand)	Spontaneous abortions	Spontaneous abortion rate (%)
1-1,000	11	353	3	8.50	13	3.68
1,001-5,000	38	4,073	41	10.07	207	5.08
5,001-10,000	13	3,927	29	7.38	236	6.01
>10,000	9	9,460	62	6.55	606	6.40

In 35 settlements the arsenic level of drinking water was below 10 μg/L. Taking this as a reference value, the incidence rate ratios (and their 95% confidence intervals) of spontaneous abortions (corrected for the number of inhabitants) were significantly increased above 20 μg/L concentrations. (Table 8.) Similar association between the arsenic concentrations and the incidence of stillbirths could not be observed. (Table 9).

Table 8. Risk of stillbirth (SB) above various concentrations of arsenic in the drinking water

As conc. cut-off point (µg/L)	Settlements above/below cut-off point	Live births above/below cut-off point	Number of SB above/below cut-off point	SB rates (per 1 thousand) above/below cut-off point	Crude Relative Risk RR (95% CI)	P value	Incidence Rate Ratio adjusted to population size RR (95% CI)	P value
10	36/35	11,335/6,478	83/52	7.3/8.0	0.91 (0.65-1.29)	0.60	1.04 (0.72-1.51)	0.823
15	27/44	9,655/8,158	69/66	7.1/8.1	0.88 (0.63-1.24)	0.47	1.00 (0.70-1.43)	0.999
20	13/58	3,509/14,304	30/105	8.5/7.3	1.16 (0.78-1.74)	0.46	1.27 (0.83-1.93)	0.271
25	9/62	2,892/14,921	24/111	8.3/7.4	1.11 (0.72-1.73)	0.63	1.21 (0.77-1.90)	0.404
30	7/64	1,374/16,439	9/126	6.6/7.7	0.86 (0.44-1.68)	0.66	0.86 (0.43-1.69)	0.656

Table 9. Risk of spontaneous abortions (SpAB) above various concentrations of arsenic in the drinking water

As conc. cut-off point (µg/L)	Settlements above/below cut-off point	Live births above/below cut-off point	Number of SpAB above/below cut-off point	SpAB rates (%) above/below cut-off point	Crude Relative Risk RR (95% CI)	P value	Incidence Rate Ratio adjusted to population size RR (95% CI)	P value
10	36/35	11,335/6,478	677/385	5.18/5.23	1.00 (0.89-1.13)	0.94	0.94 (0.83-1.08)	0.383
15	27/47	9,655/8,158	588/474	5.36/5.11	1.05 (0.93-1.18)	0.46	0.99 (0.87-1.12)	0.844
20	13/58	3,509/14,304	244/818	5.82/5.07	1.20 (1.05-1.38)	0.009	1.16 (1.001-1.34)	0.048
25	9/62	2,892/14,921	208/854	6.03/5.09	1.24 (1.07-1.44)	0.004	1.20 (1.03-1.42)	0.022
30	7/64	1,37416,439	102/960	6.03/5.11	1.25 (1.03-1.53)	0.030	1.23 (1.01-1.52)	0.043

DISCUSSION

The arsenic level of drinking water in the study area has some special features. The first one is that neighbouring villages can have drinking water with very different arsenic level depending on the depth of the wells supplying the drinking water. This explains that in settlements supplied with drinking water of high or low arsenic content, the way of life and other environmental risk factors do not differ significantly from each other.

The second feature is that in several settlements more than one well is connected to the drinking water network. Therefore, depending on the seasonal variations of water demand, various mixing ratios of water from different sources may result in changing levels of arsenic in the water of the same settlement. Moreover, due to the ecological type of these studies exposure assessment was done on settlement level and the individual characteristics of exposure could not be considered. All these may, naturally, cause uncertainty in the exposure estimation. However, the improving statistical data on pregnancy outcomes with decreasing level of arsenic in drinking water support our findings on the associations between adverse pregnancy outcomes and arsenic level of drinking water.

Summing up the findings of our studies, we can conclude that, in spite of their ecological design, our studies provided evidence on the associations between the arsenic level of drinking water and some adverse pregnancy outcomes, first of all, spontaneous abortions.

REFERENCES

Börzsönyi M, Bereczky A., Rudnai P., Csanády M. and Horváth A.(1992) Epidemiological studies on human subjects exposed to arsenic in drinking water in Southeast Hungary. *Arch Toxicol* 66:77-78.

Gulyás E. and Rudnai P. (1997) Adverse effects of drinking water related arsenic exposure on some pregnancy outcomes in Karcag, Hungary. (in Hungarian) *Egészségtudomány* 41, 137-44.

Rudnai P. and Deák Zs. (1988) Epidemiological study on the health effects of drinking water with high arsenic content. (in Hungarian) In: A környezet arzén szennyezettségének településegészségügyi kérdései a dél-alföldi régióban. (ed by I. Dési) Szeged, pp. 63-68.

Rudnai P., Varró M.J., Borsányi M, Páldy A, von Hoff K, Sárkány E. and Szép H (2006) Arsenic in drinking water and pregnancy outcomes: an ecological study. *Epidemiology* 17(6 Suppl):S329-330.