Risk of arsenic-related skin lesions in Bangladeshi villages at relatively low exposure: a report from Gonoshasthaya Kendra

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Objective Arsenic concentrations in 25% of tube wells in Bangladesh exceed 50µg/L, a level known to be hazardous. Levels in individual wells vary widely. We gathered data on arsenic exposure levels and skin lesion prevalence to address the lack of knowledge about risks where the average arsenic concentrations was lower.

Methods The nongovernmental organization Gonoshasthaya Kendra did three related studies of keratotic skin lesions since 2004: (1) an ecological prevalence survey among 13 705 women aged ⩾ 18 in a random sample of 53 villages; (2) a case-control study of 176 cases and age- and village-matched referents; and (3) a prevalence survey of the entire population of 11 670 in two additional villages. We calculated prevalence as a function of average arsenic concentrations as reported in the National Hydrochemical Survey, and measured arsenic concentrations in wells used by subjects in the case-control study.

Findings The prevalence of skin lesions was 0.37% in people exposed to arsenic concentrations below 5µg/L, 0.63% at 6–50µg/L, and 6.84% at 81µg/L. In the case-control analysis, relative risk of skin lesions increased threefold at concentrations above 50µg/L ($P < 0.05$).

Conclusion Little serious skin disease is likely to occur if the arsenic concentration in drinking water is kept below 50µg/L, but ensuring this water quality will require systematic surveillance and reliable testing of all wells, which may be impractical. More research is needed on feasible prevention of toxic effects from arsenic exposure in Bangladesh.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Arsenic is a human carcinogen and skin pathogen; the evidence has been documented by the International Agency for Research on Cancer on several occasions.[1] A potentially serious threat to public health that has become evident during the last 30–40 years is natural arsenic contamination of drinking water, notably in South America and Asia and more recently in Bangladesh and West Bengal (India). Toxic manifestations have been primarily keratotic skin lesions; more threatening, however, are internal cancers, for which there is less certain evidence.[2] A major national disaster was evidenced by the publication in 2001 of a systematic survey of nearly 4000 wells[3] showing that half Bangladesh's administrative districts had average arsenic concentrations above – often well above – 50µg/L, a level known to be hazardous. These averages may be a poor reflection of the problem, as levels varied enormously within and between villages by several orders of magnitude. Thus it is virtually impossible to estimate what proportion of Bangladesh's rural population is at risk even at the national standard of 50µg/L, let alone above the WHO recommended guideline of 10µg/L. Given this extremely varied pattern of exposure, there is need for epidemiological data over a wide range of concentrations.

There have been five recent prevalence studies: one in West Bengal,[4] later used in a case-control analysis,[5] and four in Bangladesh,[6–9] where exposures estimated individually were related to risk of skin lesions. Two studies[6–7] reported very low risks below 50µg/L, rising to prevalences of 20–30% at higher concentrations. The two remaining studies by Ahsan et al.[8] and Rahman et al.[9] published in 2006 were both large and from circumscribed areas south-east of Dhaka, where arsenic contaminations are high. The former study, in Araihazar, reported a systematic increase in prevalence odds ratios (OR) compared to those in drinking water containing <8.1µg/L, of 1.91 at 8.1–40µg/L, rising to 5.39 at > 175.1µg/L. Rahman et al. did not present comparable data on exposure-response in Matlab, but the overall prevalence in adults was only 4/1000 after an average of some 20 years' tube-well use, and a mean exposure of 167µg/L. The apparent difference between the findings in these two studies and others is addressed below.

Research objectives

Uncertainties over levels of risk at relatively low arsenic concentrations seriously concern Gonoshashthaya Kendra (GK), a large NGO long known internationally for innovations in health care.[10] GK provides comprehensive services for the entire population of over a million in some 600 villages spread across much of the country, excepting the divisions

of Khulna in the south and Sylhet in the north-east. Only 3% of GK's villages are in districts with average concentrations above 50μg/L, and half in districts below 11μg/L. GK is thus well-placed to study the effects of relatively low average exposures, although such studies are complicated by the wide variations within and between villages. GK is also concerned that the risk is not confined to skin lesions, and in particular about possible effects in pregnancy and internal cancers, both of which it has begun to investigate. First, however, it was thought important to assess the risk of skin lesions at levels prevailing in the villages for which it is responsible and which are typical of much of Bangladesh.

Methods

Selection of villages, together with training and supervision of paramedics, was described in a preliminary report.[11] Cases were defined as women with one or more nodules or characteristic skin thickening on palms or soles, recorded and graded by specially trained village paramedics. No account was taken of ulceration or lesions elsewhere, and questions of diagnosis or causation were deliberately avoided. Prevalence rates by age were calculated against average concentrations reported by the National Hydrochemical Survey (NHS)[3] based on 129 wells tested in the upazillas (sub-districts) where the study villages were located.

To assess relative risk within villages, each of the 176 women with skin lesions identified in the initial survey was matched on age (+/− 5 years) with one unaffected referent (randomly chosen within age strata) in the same village. At a visit by one of this paper's authors in 2005–6 to the 27 villages with one or more case-control pairs, tube wells currently used by subjects were identified and a record made of how long each woman had used this water source. Photographs were taken of the lesions in all reported cases for later evaluation, and three water samples from each well were tested using the Arsenator equipment used in the NHS, which provided a digital readout of arsenic concentration. In the NHS, a comparison was made between the Arsenator and British Geological Survey (BGS) laboratory results based on some 250 samples in the Manduri village survey.[3] No evidence was found of any systematic difference

between the two sets, details of which are presented in the NHS.

The same survey procedure was followed in the study of two large Rajshahi villages, A and B. As these villages were new to GK, a census of all residents was the first step. Of the total population listed ($n = 11\,670$), 11 021 (94%) were examined by a paramedic, including children under five if the mothers had noticed any skin abnormalities. This survey sought to assess prevalence in males and females over the full age range. Several young children were seen, but none showed significant signs. A comprehensive study of arsenic levels in some 1400 tube wells in these two villages is in progress, with sites of each well and house addresses of each case, as determined by the Global Positioning System. These findings will be reported separately.

Statistical procedures

Prevalence (%) was calculated by age and upazilla for the 53 villages in the initial survey, and by age and sex in the study of the two special villages; χ^2 statistics with tests for trend were calculated to investigate differences in prevalence by upazilla grouped by arsenic concentration. Conditional logistic regression was used to determine the relation with exposure (highest of three concentrations recorded) in the case-control study. Prevalence odds ratios associated with age, sex and village were calculated by logistic regression in the report on the special villages.

Results

These three surveys' essential findings are summarized in Tables 1–3. Table 1 shows the prevalence of skin lesions was low (0.37%) among 6448 women living in upazillas A-E (25 villages) with an average arsenic concentration of 5μg/L or less. It was 0.63% among 5547 women in upazillas F-K (21 villages), average concentration 16–50μg/L, but very much higher (6.84%) among 1710 women in upazilla L (7 villages) with an average concentration of 81μg/L. While the range of average concentrations in the first group was narrow (0–9μg/L), that in the three higher groups (F-L) was very wide indeed (0–166μg/L). Recorded data from 33 wells in the same union helped to narrow the range (see Table 1); however, only the values from all wells measured in each upazilla are used in the present paper.

The case-control study, potentially based on 176 pairs (352 women), was finally reduced to 155 pairs by the loss of 21 cases: 14 women had moved elsewhere, and seven were unwilling to participate or not available. The results in Table 2 correlate well with those on prevalence in Table 1, showing a three-fold increase at over 50μg/L ($P < 0.05$), and some indication of an increase above 10μg/L. As cases and controls were matched for village and age, the relative risks show only the effect of differing exposure within and not between villages, and not in duration to the extent that age is a reliable surrogate. A further analysis of pairs aged over and under 40 years (not shown) suggests that the relative risks were similar in older and younger women.

Table 3, based on the two large villages, shows that the overall prevalence was over twice as high in Village B (3.2%) as in Village A (1.3%); it was fairly similar in men and women in Village B, but less so in Village A. Prevalence in both villages rose sharply with age, with rates somewhat higher in men than in women. Cases in children were very rare. A logistic regression, excluding those aged 5 years or less (and those with unknown age) confirmed ($P < 0.001$) the higher risk in village B (OR = 2.44, 95% CI: 1.74–3.41) and the increasing risk with age (OR = 1.034, 95% CI: 1.027–1.042): the observed slight increase in prevalence in men was not significant in this model (OR = 1.19, 95% CI: 0.87–1.62). In women over 30, in Village B, the average prevalence (5.2%) approximated that in upazilla L (Table 1). Of the 10 wells recorded in the upazilla in which these two villages A and B were located, only one showed a concentration above 1.1μg/L (57.8μg/L in Village A). In our ongoing survey, however, many wells in both villages had concentrations above 100μg/L.

Discussion

The main epidemiological problems in assessing the arsenic hazard in Bangladesh are in exposure estimation at the individual or household level, and in identifying potentially related disease. The commonly observed gradient with age in prevalence studies suggests that except perhaps in pregnancy, risk is determined by both arsenic concentration in drinking water and duration of consumption over at least 20 years. To assemble such data reliably for a large study

Table 1. **Skin lesion prevalence (%) in 12 upazillas by average arsenic concentration (µg/L)**

Upazilla	Villages *n*	Wells tested *n*	Average µg/L	Range µg/L	Wells in same union[a]		Women *n*	Cases *n*	Prevalence (%)
					n	mean			
A	8	11	<1	0–2	2	0	2431	9	
B	3	8	<1	0–1	2	0	751	4	
C	4	7	1	0–5	2	1	570	1	
D	1	8	1	0–9	5	2	407	0	
E	9	8	5	0–7	–	–	2289	10	
A–E	25	42	1	0–9 (0%)[b]	11	1	6448	24	0.37
F	3	10	16	0–63	3	17	551	7	
G	4	12	16	0–115	4	3	1236	6	
H	3	9	19	0–64	4	46	1178	6	
I	1	8	21	0–107	2	5	99	0	
F–I	11	39	19	0–115 (13%)[b]	13	19	3064	19	0.62
J	7	14	39	2–118	3	46	1956	13	
K	3	8	50	10–81	1	31	527	3	
J–K	10	22	43	2–118 (41%)[b]	4	42	2483	16	0.64
L	7	10	81	2–166 (70%)[b]	2	50	1710	117	6.84
Total	53	113	21	0–166	30	18	13 705	176	1.28

[a] Included in upazilla average.
[b] Proportion of wells above 50µg/L.

population would be extremely difficult and, as mentioned earlier, was attempted by Haque et al.[5] in West Bengal, where the mean arsenic concentration was 185µg/L (range 0–3400µg/L). A nested case control study limited to 21 villages in which the primary drinking-water sources contained < 500 µg/L had only limited success in estimating past exposure, but the odds ratio in relation to peak concentration of < 50µg/L was 2.4 at 50–99µg/L, a result close both to our own from a similar nested study (2.96) and to that reported by Ahsan[8] (3.03) for exposures in the range 40–91µg/L.

Because the assessment of individual exposures is so difficult, we opted initially for an ecological approach for assessing prevalence, using data from the National Hydrochemical Survey.[3] This survey of almost 4000 wells used a systematic grid resulting in one well tested each 37km², but amounted to only about 60 wells per district and 8 per upazilla for the calculation of averages. Although the geographical pattern of arsenic concentrations after statistical smoothing appeared clear, this obscured enormous local variations. For example, in three special survey areas concentrations ranged from < 3 to 2542µg/L. Even in the upazilla where Villages A and B are located, despite an average of 6µg/L, the only well tested in Village A had a level of 57.8µg/L. Thus the

ecological approach, though useful, has limitations.

A further difficulty lies in the ascertainment of skin lesions. Whereas we relied on paramedics to describe objectively the results of simple inspection, other studies[4–8] have used physicians exercising their varying levels of judgement, and in one[9] (Matlab, Bangladesh) expert panels of physicians and dermatologists were used to reach consensus on the diagnosis of arsenical keratosis. This resulted in rejection of 70% of cases reported by the field workers. This alone may largely explain the differences between their rates and others, including ours, though it is worth noting that the average exposure in Matlab was 167µg/L, and only our upazilla L (Table 1) had values approaching that

level, though with a wide range in values for the 10 wells tested (2–166µg/L). Also relevant is the fact that the average duration of tube-well use in Matlab was about 20 years, whereas most of the wells in upazilla L were reported to date from 1953, up to 50 years earlier than our survey.

An important purpose of the 53-village prevalence study was to evaluate the published ecological data[3] and adequacy of the national standard of 50µg/L in assuring safety. Table 1 suggests that the number of cases in groups A-E was probably negligible, and in group L, in clear excess. The interpretation of groups F-I and J-K is more difficult. The prevalence rates are almost double the lowest group (*P* = 0.04), but the average concentrations in both

Table 2. **Risk of skin lesions by arsenic concentration in drinking water (conditional logistic regression)**

Arsenic[a] concentration (µg/L)	Cases		Controls		Odds ratio	95% CI
	n	%	*N*	%		
0–10	85	54.8	97	62.6	1	–
11–50	53	34.2	49	31.6	1.33	0.77–2.28
51+	17	11.0	9	5.8	2.96	1.02–8.59
All	155	100.0	155	100.0	–	–

CI, confidence interval.
[a] Highest measured concentration.

Table 3. **Skin lesion prevalence (%) by age and sex in two neighbouring Rajshahi villages**

Age	Village A[a]			Village B[a]		
	M	**F**	**All**	**M**	**F**	**All**
≤ 5	0/369 (0.0)	0/383 (0.0)	0/752 (0.0)	0/373 (0.3)	0/344 (0.0)	0/717 (0.0)
6–17	5/854 (0.8)	1/776 (0.1)	6/1630 (0.4)	2/903 (0.2)	5/745 (0.7)	7/1648 (0.4)
18–30	8/725 (1.1)	5/806 (0.6)	13/1531 (0.8)	17/814 (2.1)	6/824 (0.7)	23/1638 (1.4)
31–50	12/715 (1.7)	9/641 (1.4)	21/1356 (1.5)	26/647 (4.2)	29/577 (5.0)	55/1224 (4.5)
51–70	5/257 (1.9)	3/207 (1.4)	8/464 (1.6)	20/283 (7.1)	12/226 (5.3)	32/509 (6.3)
≥ 71	1/32 (3.1)	0/55 (0.0)	1/87 (1.1)	1/77 (1.3)	1/31 (3.2)	2/108 (1.9)
Unknown	0/3 (–)	1/3 (–)	0/6 (–)	0/3 (–)	0/3 (–)	0/6 (–)
Total	**31/2952 (1.1)**	**18/2868 (0.6)**	**49/5820 (0.8)**	**66/3100 (2.1)**	**53/2750 (1.9)**	**119/5850 (2.0)**
≥ 18	**26/1729 (1.5)**	**17/1568 (1.1)**	**43/3297 (1.3)**	**64/1824 (3.5)**	**48/1661 (2.9)**	**112/3485 (3.2)**

[a] In each of the six columns, the sequence is: cases/subjects, followed by prevalence (%) in parenthesis.

are below 50µg/L. However, in these groups there is evidence that in 14 of 61 wells (23%) the level was above 50µg/L, suggesting a potential risk. The exposures used for classifying subjects for our case-control analysis were measured by Arsenator, and so were comparable to the BGS data used to classify the 53 villages in Table 1. A detailed analysis, not shown, of the 310 well measurements used for Table 2 indicated that most of the values above 50µg/L were from subjects in upazilla L, and only a few from upazillas F–K.

It was said that arsenic levels and skin lesion prevalence were higher in the upper socioeconomic sections of the Matlab populations.[9] We therefore examined this question using GK's plentiful data on social factors. It was not possible to do this for the villages individually, but we examined the main geographical groups to which our 53 villages belonged and selected as the best available index the proportion of pregnant women in the last two years classified as poor or very poor. The resulting proportions in the four arsenic concentration categories used in Table 1 were as follows: A–E 77%; F–I 86%; J–K 88%; L 78%. There was clearly no systematic trend. Other confounders such as smoking, occupation and sunlight were identified by Chen et al.[12] as important in explaining the higher prevalence in men. This was not considered important in our 53-village study, as this was confined to adult women.

Our studies have both strengths and weaknesses, the most important of the former being that they have successfully evaluated risk in the total adult female population of 53 villages, randomly selected and widely scattered, at moderate levels of exposure. However, the skin lesions recorded by trained paramedics were not further validated. We are confident nevertheless that any excess risk in areas of the country where the average arsenic concentration was below 10µg/L is most unlikely. There is evidence of a small risk in areas with averages between 11 and 50µg/L, probably explained by wells in which 50µg/L was exceeded. Above 50µg/L, though our data at higher concentrations are scanty, the risk appears substantial. It is reasonably certain that the prevalence of skin lesions recorded in three of the seven villages in upazilla L was very high (102 cases in 772 women – 13%), a sample of whom were examined and confirmed by three of us (NC, NH and JCMcD). This level of risk was quite compatible with rates recorded in villages A and B of the supplementary survey in Rajshahi (Table 3).

If we are correct in these conclusions, it follows that public health policy in areas of the country at relatively low exposure should give priority to ensuring that the concentration of arsenic in water actually used for drinking is kept below 50µg/L. This would require reliable and systematic testing, retesting, marking and perhaps closing of all offending hand-pump tube wells, together with continued skin lesions surveillance. Such measures should be possible in most of the country, but in

areas where the average concentration exceeds 50µg/L this policy may be inadequate or unfeasible, in which case more radical measures would be needed; these are beyond the scope of this paper. However, until it is known whether the lifetime ingestion of water containing arsenic below 50µg/L carries a significant risk of internal cancers or important adverse effects in pregnancy, no public health policy can be final. ∎

Ethical issues
The study protocol was formally approved by the Ethics Committee of the Royal Brompton Hospital, London. In addition, research plans were approved by the GK Executive Committee, the body responsible for all health services in GK villages.

Competing interests: None declared.

Résumé

Risque de lésions cutanées liées à l'arsenic dans des villages du Bengladesh relativement peu exposés à ce métal : rapport de l'organisation Gonoshasthaya Kendra

Objectif Dans 25 % des puits tubulaires du Bengladesh, la concentration d'arsenic dans l'eau dépasse 50 µg/l, un niveau connu pour être dangereux. Les concentrations d'arsenic varient fortement d'un puits à l'autre. En réponse au manque de connaissances sur les risques dans le cas de concentrations moyennes d'arsenic plus faibles, nous avons collecté des données sur les niveaux d'exposition à l'arsenic et sur la prévalence des lésions cutanées.

Méthodes L'organisation non gouvernementale Gonoshasthaya Kendra a réalisé trois études sur les lésions cutanées kératosiques depuis 2004 : (1) une enquête de prévalence écologique chez 13 705 femmes âgées de 18 ans et plus appartenant à un échantillon aléatoire de 53 villages, (2) une étude cas-témoins portant sur 176 couples cas/témoins appariés en fonction de l'âge et du village ; et (3) une enquête de prévalence dans l'ensemble de la population (11 670 personnes) de deux autres villages. Nous avons calculé la prévalence en fonction des concentrations moyennes d'arsenic rapportées par la National Hydrochemical Survey et mesuré la concentration d'arsenic dans les puits utilisés par les sujets de l'étude cas-témoins.

Résultats La prévalence des lésions cutanées était de 0,37 % chez les personnes exposées à des concentrations d'arsenic inférieures à 5 µg/l, de 0,63 % pour des niveaux d'exposition de 6 à 50 µg/l et de 6,84 % pour un niveau d'exposition de 81 µg/l. L'analyse des données de l'étude cas-témoins relève une augmentation d'un facteur trois du risque de lésions cutanées au-dessus de 50 µg/l (p < 0,05).

Conclusion Tant que la concentration d'arsenic dans l'eau de boisson est maintenue à une valeur inférieure à 50 µg/l, la probabilité que ce métal entraîne des lésions cutanées graves reste faible. Cependant, garantir une telle qualité de l'eau nécessite une surveillance systématique et une analyse fiable de tous les puits, ce qui peut être impraticable. Des études plus poussées sont nécessaires pour établir la faisabilité de la prévention des effets toxiques de l'exposition à l'arsenic au Bengladesh.

Resumen

Riesgo de lesiones cutáneas relacionadas con el arsénico en pueblos de Bangladesh con una exposición relativamente baja: un informe de Gonoshasthaya Kendra

Objetivo Las concentraciones de arsénico en el 25% de los pozos entubados de Bangladesh superan los 50 µg/l, nivel que se considera peligroso. Las concentraciones varían mucho de un pozo a otro. Para conocer mejor los riesgos en lugares con menores concentraciones medias de arsénico, hemos reunido datos sobre los niveles de exposición al arsénico y la prevalencia de lesiones cutáneas.

Métodos Desde 2004, la organización no gubernamental Gonoshasthaya Kendra ha llevado a cabo tres estudios conexos sobre las lesiones cutáneas queratósicas: 1) un estudio ecológico de prevalencia en 13 705 mujeres de 18 años o más de una muestra aleatoria de 53 pueblos; 2) un estudio de 176 casos y otros tantos controles apareados por edad y pueblo de residencia, y 3) un estudio de prevalencia en los 11 670 habitantes de otros dos pueblos. Se calculó la prevalencia en función de las concentraciones medias de arsénico registradas en la Encuesta Hidroquímica Nacional y de las concentraciones de arsénico medidas en los pozos utilizados por los participantes en el estudio de casos y controles.

Resultados La prevalencia de lesiones cutáneas fue del 0,37%, 0,63% y 6,84% en personas expuestas a concentraciones de arsénico inferiores a 5 µg/l, de 6–50 µg/l y de 81 µg/l, respectivamente. En el estudio de casos y controles, el riesgo relativo de lesiones cutáneas se multiplicó por tres con concentraciones superiores a 50 µg/l (P < 0,05).

Conclusión Si la concentración de arsénico en el agua potable se mantiene por debajo de 50 µg/l, es poco probable que se produzcan lesiones cutáneas graves, pero para garantizar esta calidad del agua se necesitan una vigilancia sistemática y análisis fiables de todos los pozos, lo cual puede resultar poco viable en la práctica. Son necesarias más investigaciones sobre la prevención factible de los efectos tóxicos de la exposición al arsénico en Bangladesh.

ملخص

مخاطر حدوث الآفات الجلدية ذات الصلة بالزرنيخ في قرى بنغلاديش المتعرِّضة لمستوى منخفض نسبياً منه: تقرير لمنظمة غونوشستايا كندرا

الملخص: يزيد تركيز الزرنيخ في 25% من الآبار الأنبوبية في بنغلاديش على 50 مكروغرام/لتر، وهو مستوى يتَّسم بالخطورة. وتتفاوت مستويات التركيز تفاوتاً كبيراً من بئر إلى أخرى. وقمنا في هذه الدراسة بجمع بيانات عن مستويات التعرُّض للزرنيخ ومعدل انتشار الآفات الجلدية، بُغْيَةَ التصدِّي لنقص المعلومات عن المخاطر المحتملة حال انخفاض التركيزات المتوسطة للزرنيخ.

الطريقة: أجرت منظمة غونو شستايا كندرا ثلاث دراسات مترابطة للآفات الجلدية التقرانية منذ عام 2004، شملت: (1) دراسة مسح إيكولوجي لمعدل انتشار الآفات بين 13705 امرأة في عمر 18 عاماً أو أكثر، وذلك في عيِّنة عشوائية من القرى عددها 53 قرية؛ (2) دراسة للحالات والشواهد شملت 176 حالة متماثلة في العمر ومن نفس القرية؛ (3) دراسة مسح لمعدل انتشار الآفات بين إجمالي السكان البالغ عددهم 11670 نسمة في قريتَيْن إضافيتَيْن. وتم حساب معدلات الانتشار كدالة للتركيزات المتوسطة للزرنيخ وفقاً للمسح الوطني للمياه والكيماويات، وتم قياس تركيزات الزرنيخ في الآبار المستخدمة من قِبَل حالات الدراسة.

الموجودات: بلغ معدل انتشار الآفات الجلدية 0.37% لدى المتعرِّضين لتركيزات من الزرنيخ تقل عن 5 مكروغرام/لتر، و0.63% لدى المتعرضين

الزرنيخ في مياه الشرب عن 50 مكروغرام/لتر. غير أن تأكيد جودة هذه المياه يتطلَّب ترصداً منهجياً واختبارات يعول عليها لجميع الآبار، وهو أمر قد يصعب تطبيقه عمليا. ويستلزم الأمر مزيداً من البحوث المجدية حول سُبُل الوقاية من التأثيرات السامة الناجمة عن التعرُّض للزرنيخ في بنغلاديش.

لتـركيزات تتـراوح من 6 إلى 50 مكروغرام/لتر، و6.84% للتركيز 81 مكروغرام/لتر. وبيَّن تحليل الحالات والشواهد ازدياد المخاطر النسبية المحتملة للآفات الجلدية بمقدار ثلاثة أضعاف في التـركيزات التي تـزيد على 50 مكروغرام/لتـر (P > 0.05).

الاستنتاج: من غير المرجَّح أن تحدث أمراض جلدية خطيرة إذا قل تـركيز

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