

Endemic goitre in the absence of iodine deficiency in schoolchildren of the Northern Cape Province of South Africa

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Objective: The study was undertaken to investigate whether endemic goitre still exists in the Northern Cape Province of South Africa more than 55 years after it was reported and, if so, whether iodine deficiency, or fluoride in the drinking water, is linked to the goitres.

Design: Cross-sectional study of children in three pairs of towns.

Subjects: The 6-, 12- and 15-year-old children ($n = 671$) who had been lifetime residents in two Northern Cape towns with low levels, two towns with near optimal levels and two towns with high levels of fluoride in the drinking water were recruited through the schools as study participants.

Results: Endemic goitre was found in all the towns except one, ranging from 5% to 29%. Iodine deficiency did not prevail in the study area because the median urinary iodine concentration, exceeding $1.58 \mu\text{mol/l}$ in all but one of the towns, indicated a more than adequate iodine consumption. The drinking water and, to a lesser extent, iodised salt were important sources of iodine. No relationship was found between fluoride in the water and the mild goitre prevalence (5% to 18%) in the four towns with either a low or near optimal fluoride content in the water. The causal factor(s) responsible for the goitres in these four towns were not clear from our data. However, the prevalence of goitre was higher (28% and 29%) in the two towns with high levels of fluoride in the water.

Conclusion: These results indicate that either a high fluoride level in the water or another associated goitrogen, other than iodine deficiency, may have been responsible for these goitres.

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Descriptors: fluoride; goitre; goitrogens; iodine; water

Introduction

Endemic goitre, prevailing in many countries of the globe, is usually caused by iodine deficiency (Delange, 1994; Hetzel, 1996). However, in some areas endemic goitre could also be caused or aggravated by substances found in certain foods or water that are collectively termed goitrogens. Goitrogens are substances that produce an increase in the size of the thyroid gland by interfering with the normal production of thyroid hormone (McLaren & Alexander, 1979). A number of goitrogens have been reported in the literature, some of which occur as naturally occurring precursors of goitrogenic substances in food-stuffs, others in certain drugs, or as dietary elements found in drinking water (McLaren & Alexander, 1979).

Limited information is available on the distribution, intensity and causes of endemic goitre in South Africa. Recent studies have revealed that endemic goitre induced by iodine deficiency exists in different geographical areas of the country (Jooste *et al*, 1997; Benadé *et al*, 1997). In 1955 Steyn *et al* published their report on endemic goitre in a number of geographical areas in South Africa, one of which was in the Northern Cape. These authors believed that endemic goitre was due to high fluoride levels in the drinking water of the north-western part of the Northern

Cape, and in the north-eastern parts of the province it was due to iodine deficiency. Unfortunately urinary iodine excretion was not determined in those days and the causal role of iodine and fluoride in the endemic goitre observed in these areas was indirectly based on the concentration of these halogens in the drinking water.

A dental survey of schoolchildren in six towns in the Northern Cape, with graded levels of fluoride in their drinking water, afforded us the opportunity to conduct a goitre study in this province. The aims of this study were to establish, after more than 55 years following the first report of a possible link between fluoride in water and endemic goitre in this area (Steyn 1939, 1948), whether endemic goitre still exists in this area and, if so, whether iodine deficiency or fluoride levels in the drinking water are related to the goitres.

Methods

This study was undertaken in collaboration with the Department of Community Dentistry of the University of Stellenbosch, which conducted a cross-sectional survey of oral health and fluorosis of children in six towns in the Northern Cape Province. The study population consisted of all the 6-, 12- and 15-year-old schoolchildren who had spent their entire lives in the respective towns of Victoria West, Williston, Carnarvon, Frazerburg, Kenhardt and Brandvlei. These towns were selected to represent two

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owns (Victoria West and Williston) with sub-optimal, two towns (Carnarvon and Fraserburg) with near optimal, and two towns (Kenhardt and Brandvlei) with supra-optimal levels of fluoride in the municipal supply of drinking water. Sub-optimal fluoride levels were 0.3 ppm (mass/mass) in Williston and 0.5 ppm in Victoria West, near optimal levels were 0.9 ppm in Fraserburg and 1.1 ppm in Carnarvon, and supra-optimal levels were 1.7 ppm in Brandvlei and 2.6 ppm in Kenhardt.

Demographic information of date of birth, gender and town of residence was obtained from the school records. Anthropometric measurements were carried out by weighing the children on a calibrated load cell operated electronic scale accurate to 50 g (UC-300 Precision Health Scale, Mass Measuring Systems, Cape Town, South Africa) while they were dressed in light clothing without shoes, and measuring body heights with a staturimeter containing a metal tape accurate to 0.1 mm (Trust Hospital Supplies, Cape Town, South Africa). This anthropometric data was analysed with the Epi-Info 5 software package and using the National Center for Health Statistics (NCHS) as reference population (Hamill *et al*, 1979). The proportions of children in each town with *z*-scores less than minus two standard deviations of the median of the reference population of height-for-age and weight-for-age were calculated.

The same clinician palpated the thyroid of each child in all the towns and categorised the size of the thyroid according to the World Health Organisation (WHO), United Nations Children's Fund (UNICEF) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) criteria (World Health Organisation, 1994) as normal (grade 0), palpable but not visible (grade 1) or visible and palpable (grade 2).

A casual 20 ml urine sample was obtained from each participant during school hours and stored below 4°C until analysed. These samples were analysed by means of manual acid digestion followed by the Sandell–Kolthoff reaction recorded spectrophotometrically (Sandell & Kolthoff, 1937; Dunn *et al*, 1993). The urine samples with values exceeding 1.58 µmol/l (the nonsensitive range of this method) were unfortunately not diluted and re-analysed to provide quantitative estimations of urinary iodine levels, but the median urinary iodine concentrations were used to indicate iodine deficiency or sufficiency. This method has a coefficient of variation of 4.7% at a mean urinary iodine concentration of 1.05 µmol/l (0.05 µmol/l standard deviation) in our hands. At the time of this study our laboratory participated successfully in an international quality control programme for iodine analysis organised by the Programme Against Micronutrient Malnutrition

(PAMM) of the Centres for Disease Control in Atlanta, GA, USA.

A short questionnaire was sent to each household to obtain information from the mothers regarding the use of iodised or non-iodised salt as table salt and for cooking purposes. The questionnaire also tested the knowledge of the mother about the health benefit of iodised salt. Between three and five salt samples (500 g) were purchased at grocers in each of the towns where the study was conducted. These salt samples were analysed for the iodine content using an iodometric titration method (Mannar & Dunn, 1995). A drinking water sample from the municipal water supply was also collected in each of the towns and analysed for iodine concentration using the same method as that for urinary iodine analysis. A Spearman correlation was computed between the fluoride concentration in the drinking water of each of the towns and the goitre rates in the schoolchildren.

Permission to conduct the study was obtained from the educational authorities, headmasters and parents. Ethical approval for conducting the study was obtained from the Ethics Committee of the University of Stellenbosch.

Results

In total 671 children, ranging from 85 to 183 children per town, were included in the study (Table 1). Because some of the sample sizes of the 6-, 12- and 15-year-old children were small (less than 50) and because the proportional distribution of these age subcategories was approximately similar in the different towns, these subcategories were combined within towns to provide more stable prevalence rates of the different variables in this study. Although not quantified, the response rates in the different towns were estimated to be well in excess of 90%, based on the high-school attendance rates and the fact that virtually all the eligible children participated in the study.

The proportions of children below minus two standard deviations of the median of the NCHS reference tables of the height-for-age and weight-for-age were used as indicators of nutritional status in this study. In five of the six towns these proportions generally varied between 30% and 40%, with four estimates exceeding 40%, for both these variables (Table 1). Carnarvon was the only exception, where around 23% of children were below minus two standard deviations for both height-for-age and weight-for-age, indicating less undernutrition than in the other towns.

The mean goitre prevalence varied from 5.2% in Carnarvon to 29% in Kenhardt (Table 1). It is interesting to note that two towns with high fluoride levels in the

Table 1 Characteristics of the study population in the six different towns

Town ^a	Sample size	Height-for-age (% < -2 s.d.)	Weight-for-age (% < -2 s.d.)	Goitre prevalence (%)	Median urinary iodine (µmol/l)	Iodine in drinking water (µmol/l)	Iodine in iodised salt (ppm)
Victoria West (LF)	127	44.7	33.8	17.3	> 1.58	> 1.58	5
Williston (LF)	85	39.2	42.9	15.3	> 1.58	0.83	28
Carnarvon (MF)	95	23.7	22.7	5.2	> 1.58	— ^b	9
Fraserburg (MF)	87	37.9	33.6	18.4	1.52	1.00	11
Brandvlei (HF)	94	41.3	43.2	27.7	> 1.58	> 1.58	5
Kenhardt (HF)	183	39.6	35.9	29.0	> 1.58	1.13	4

^aLF = low fluoride; MF = medium fluoride; HF = high fluoride.

^bNo water sample.

drinking water (Kenhardt and Brandvlei) also had the highest goitre rates compared to the other towns in the study. In three of the other four towns, where the fluoride levels in the drinking water were either low (Victoria West and Williston) or around optimal (Frazerburg), the goitre rates were close to each other, varying from 15% to 18%, while it was low (5.2%) in Carnarvon where the fluoride level was also around optimal.

Urinary iodine excretion is generally considered a definitive indicator of iodine status (World Health Organisation, 1994). In this study the median urinary iodine concentration exceeded $1.58 \mu\text{mol/l}$ in all the towns except for Frazerburg, where the median urinary iodine was just less than $1.58 \mu\text{mol/l}$ (Table 1). As median urinary iodine concentrations above $0.79 \mu\text{mol/l}$ indicate iodine sufficiency in a community, it can safely be concluded that iodine deficiency was not a public health problem in any of these towns. The distributions of urinary iodine values in each of the towns are given in Figure 1. From this figure it is evident that small percentages of children had urinary iodine levels of less than $0.79 \mu\text{mol/l}$ and that a large proportion of children in all the towns, except Frazerburg, had values exceeding $1.58 \mu\text{mol/l}$. A shortcoming of these data is the fact that urinary iodine values exceeding $1.58 \mu\text{mol/l}$ are not given quantitatively because the analytic method is not sensitive at high concentrations ($> 1.58 \mu\text{mol/l}$) and urine samples with high iodine levels were not diluted during the analyses. However, both the medians and the distributions of the urinary iodine levels in the different towns nevertheless indicated quite distinctly that iodine deficiency did not occur in this region.

The iodine concentration in samples of the municipal drinking water supply and iodised salt obtained in each of the towns are also given in Table 1. Unfortunately, a drinking water sample was not obtained from Carnarvon, but in the other towns the iodine concentration varied from $0.83 \mu\text{mol/l}$ to more than $1.58 \mu\text{mol/l}$. Iodised salt purchased at grocer shops had iodine levels that varied from low (4 ppm) to high (28 ppm) compared to the level of 10–20 ppm required by law at the time of the study. Both iodised and non-iodised salt were available in all the towns, but not in all the grocer shops that were visited. Some

grocers stocked only non-iodised salt and it appeared that generally more non-iodised than iodised salt was available in these shops.

In a short self-administered questionnaire, mothers of households with participating children were asked what type of salt (iodised or non-iodised) was used in the house. They were also asked about the health benefits of iodised salt to estimate their level of knowledge, or awareness, of the health benefit of iodised salt. A total of 491 completed questionnaires were returned, representing an overall response rate of 73.2% (not accounting for families with more than one child participating in the study) in the six towns. Of those mothers who responded either positively or negatively (excluding the 140 mothers who were uncertain), 32% said they had iodised salt in the house and the balance, 68%, did not have iodised salt. Only 2% of mothers were aware of the benefit of iodised salt, the rest either gave an incorrect answer or did not know.

Discussion

Endemic goitre prevailed among children who had been lifetime residents in the study communities, except for Carnarvon where the prevalence of goitre was low and could be considered acceptable in terms of goitre prevalence. When goitres are found in more than 5% of children in a specified study community, it is said that endemic goitre prevails in such a community and it then signals a public health problem (World Health Organisation, 1994). The severity of goitre prevalence rates in towns with either low or optimal fluoride levels in the drinking water was mild (ranging from 5.2% to 18.4%) and in the towns with high fluoride levels it was moderate (ranging from 27.7 to 29.0%) (Table 1).

Endemic goitre is, with few exceptions, usually caused by iodine deficiency in most goitrous areas of the world. However, it is known that goitrogens in food may also cause or aggravate endemic goitre (McLaren & Alexander, 1979; Gaitan, 1990). In his review, Gaitan (1990) summarised goitre endemias attributed to goitrogens in food and water in different parts of the world, for example the goitrogenic action of thiocyanate produced endogeneously from cassava, a staple food in Central Africa. High mineral content, particularly of magnesium and calcium salts, water hardness, and bacterial contamination have also been implicated as goitrogenic factors in water (Gaitan, 1990). Fluoride in water is considered by some researchers to be goitrogenic (Steyn, 1939; Steyn *et al* 1955; Siddiqui, 1960; Day & Powell-Jackson, 1972), also because goitres develop when fluoride at a high concentration is fed to animals (Steyn *et al*, 1955; Day & Powell-Jackson, 1972), but its goitrogenicity is disputed by others (Bürigi *et al*, 1984). Although goitre was associated with high levels of fluoride in drinking water, the designs of these studies were inadequate to prove a causal relationship between fluoride at a concentration recommended for caries prevention and goitre (Bürigi *et al*, 1984). Doubt therefore exists about the goitrogenicity of fluoride in drinking water because a large number of studies failed to support the view that fluoride at low or near optimal concentrations adversely affects the thyroid (Bürigi *et al*, 1984).

In our study in the Northern Cape, the goitre prevalence did not correlate with graded levels of fluoride in water in the six study towns (Spearman $r=0.66$, $P=0.16$). However, in Kenhardt and Brandvlei, where the fluoride level in

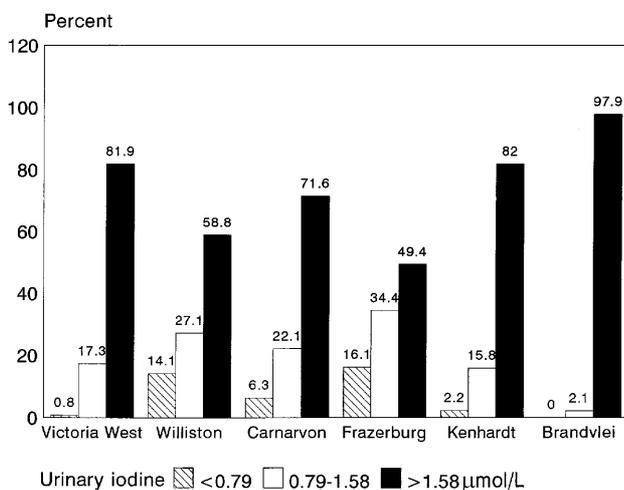


Figure 1 The distribution of urinary iodine concentration of school-children in categories of deficiency and sufficiency in six Northern Cape towns.

the water was sufficiently high to cause severe mottling of the teeth in most of the children, not seen in the other towns, the goitre prevalence was also markedly higher than in the other four towns in the study. This observation agrees with the close quantitative association between fluoride and goitre reported by Day & Powell-Jackson (1972) in children living in 13 Nepalese villages with low iodine concentrations in their water. Again it was not possible to ascribe a causal effect to the fluoride in Day & Powell-Jackson's study (1972) because significant correlations were also found between the goitre prevalence in the villages and the concentrations of calcium and magnesium, in their drinking water, as well as water hardness. It would therefore appear that fluoride has a questionable goitrogenic effect at low concentrations, but a different picture emerges at unusually high concentrations. More goitres were seen in our study in towns with a high fluoride concentration in the water. It therefore seems likely that either a high fluoride concentration itself or an associated goitrogen other than iodine deficiency, was responsible for the goitres seen in these studies. The fact that some goitres also occurred in the Northern Cape towns with low or near optimal fluoride concentrations in the water suggests that another goitrogenic factor, or combination of factors, induced these goitres.

It is interesting to note that in the present study the lowest prevalence of goitre was observed in Carnarvon, the town in which the prevalence of undernutrition, using the indicators height-for-age and weight-for-age (Table 1), was also markedly lower than in the other study towns. The reason for the lower goitre rate and more favourable nutritional status observed in Carnarvon compared to the other towns is not clear from our data. In iodine-deficient communities we found that there was a greater likelihood of endemic goitre in low socioeconomic children with a poor nutritional status (Jooste, *et al*, 1997). The more favourable nutritional status in the Carnarvon children may therefore be related either to a higher socioeconomic status or to successful nutritional intervention programmes. It is also possible that, despite their adequate iodine intake, the high rates of stunting and underweight in the other towns predisposed the children to the risk of goitre development (Gaitan, 1990). In iodine-deficient populations, undernutrition and endemic goitre frequently coexist and it appears possible from this study that it could also be the case in iodine-sufficient populations exposed to environmental goitrogens.

In view of the high median urinary iodine concentrations of children in all the towns of this study, it is evident that iodine deficiency was not involved in the pathogenesis of goitres seen in these children. The median values, exceeding 1.58 $\mu\text{mol/l}$ in all but one of the towns, actually indicated high dietary iodine intakes in this region. Excessive iodine intakes may cause *iodide goitres*, seen in some Japanese fishermen who consume iodine-rich seaweeds (Gaitan, 1990), but it is unlikely that the iodine intake of children in this study was that high. From Figure 1 it is also clear that a few of the children had urinary iodine excretions less than 0.79 $\mu\text{mol/l}$, which indicates iodine deficiency, and that the vast majority of the children had a more than adequate iodine intake. The most likely source of the high iodine intake in these children is the drinking water with high iodine concentrations, particularly in Victoria West, Kenhardt and Brandvlei (Table 1). A litre of water in these towns contains an adequate amount of iodine

to provide the daily requirement for this micronutrient (150–200 μg per day for adults, less in children (Delange, 1994)) and it is likely that the inhabitants' water intake in this hot and dry climate may be in excess of one litre per day.

The questionnaire information indicated that only 32% of households used iodised salt. It is therefore doubtful that iodised salt contributed substantially to the iodine intake, particularly in towns where the iodine in salt was less than 10 ppm. The introduction of compulsory iodisation of table salt in South Africa at the end of 1995, iodised at higher levels than before, will most likely result in a further increase in the daily iodine intake in this region with its existing adequate iodine consumption. Further research is required to investigate the effect of compulsory iodisation on the daily iodine intake and the goitre rates of children living in these Northern Cape towns.

Educating the public about iodine deficiency disorders is a complex matter against the background of the present study. The question may be asked: 'Is it worthwhile and relevant to educate the public on iodine deficiency in areas like the study towns where there is an abundance of iodine in their food chain?' From the information obtained from the mothers of households, it became clear that a very low percentage of mothers, only 2%, correctly knew the health benefit of iodine in iodised salt. It would therefore require a vigorous and costly education campaign to educate the mothers on public health issues of the prevention and control of iodine deficiency and endemic goitre. In an area of iodine sufficiency it hardly seems a cost-effective exercise to educate people about a low-cost commodity such as iodised salt.

Conclusion

In summary, endemic goitre was found in five of the six Northern Cape towns in this study. As a result of the more than adequate iodine intake reflected by the high median urinary iodine values, it is concluded that iodine deficiency was not the aetiological factor in the development of the goitres. Fluoride at low and near optimal levels in the drinking water of two pairs of towns was not associated with a graded goitre prevalence as would have been expected had fluoride been a goitrogen. Higher goitre prevalences were observed in the two towns with high levels of fluoride in the drinking water, but the design of the study precludes a causal inference. Therefore, it could be concluded that either fluoride at high concentrations may behave as a goitrogen or that the high fluoride levels were associated with another factor with goitrogenic properties.

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