

Childhood goitre in Saudi Arabia

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Summary Thirty-two Saudi children (aged 1.5-14 years) with goitre were seen over a 6.5-year period in a paediatric endocrinology clinic. There was a female to male ratio of 1.9:1. Of these, 27 (84.3%) had diffuse thyroid enlargement and five (15.7%) nodular goitre. The commonest causes were dysmorphonogenesis (37.5%) followed by Hashimoto's thyroiditis (34.4%). Three boys and one girl had Graves' disease. There were three (9.4%) with simple goitre and one case each of iodine deficiency goitre and tuberculous thyroiditis. Further study of the prevalence and causes of goitre, including iodine deficiency goitre, in Saudi Arabia is suggested.

Introduction

A goitre is an enlargement of the thyroid gland.¹ In developed countries, chronic lymphocytic thyroiditis, Graves' disease and colloid goitre, respectively, are the commonest causes of thyromegaly among children and adolescents.^{1,2} However, due to genetic and environmental factors, worldwide variation in the incidence and aetiopathogenesis of goitre has been reported.^{3,4} The objective of this retrospective study is to analyze the aetiology of goitre in children referred to the paediatric endocrinology clinic at the Security Forces Hospital, Riyadh, Saudi Arabia, to which all children under 12 years are referred. Children between 12 and 18 years may be referred either to our clinic or to adult clinics. To our knowledge, no similar data on Saudi Arabian children have been published previously.

Patients and methods

The Security Forces Hospital is a 500-bed secondary and tertiary care referral centre for all employees of the Ministry of the Interior and therefore receives cases from all over Saudi Arabia. All cases of goitre referred to or detected in the paediatric endocrinology clinic between January 1990 and June 1996 were included in this study. All records were reviewed and all relevant information including clinical and laboratory data was extracted for further analysis. Goitre was graded according to the modified World Health Organization recommendation (Table I).² Hashimoto's thyroiditis was diagnosed on clinical grounds and when positive thyroid autoantibodies were found. Graves' disease was diagnosed by diffuse thyroid enlargement associated with clinical and biochemical hyperthyroidism with and without thyroid-stimulating autoantibodies (TSI). The diagnosis of dysmorphonogenesis was based on performance of thyroid uptake and the potassium perchlorate discharge test, as described elsewhere.⁵ Thyroxine (T₄) and TSH levels were measured using the Delfia

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TABLE I. Modified WHO criteria for goitre grading (ref. 2)

Grade 1.	Easily palpable goitre not visible even with the neck extended
Grade 2.	A visibly enlarged thyroid gland when the neck is extended
Grade 3.	A visibly enlarged thyroid gland in the normal neck position
Grade 4.	A very large goitre

immunofluorescent kit (Pharmacia Diagnostic, Wallacoy, Finland). Thyroid microsomal and thyroglobulin autoantibodies were measured using MT Fluro Kit indirect fluorescent antibody test (INCSTAR Corporation, Stillwater, Minnesota, USA). A titre of $> 1:20$ was considered positive. The urinary iodine was measured on a random urine sample using the method of Wawschinek as modified by Dunn *et al.*⁶

Results

During the study period, a total of 32 children were identified as having goitre. All were Saudi nationals. Their ages ranged from 1.5 to 14 years (mean 8.8 years). There were 21 girls and 11 boys, giving a female to male ratio of 1.9:1. In 27 subjects (84.3%), there was diffuse enlargement of the gland, and only five (15.7%) had nodular thyroid enlargement. Two of these had Hashimoto's thyroiditis, and one each had dysmorphogenesis, iodine deficiency and tuberculosis. No cases of malignant thyroid disease were encountered. Thyroid enlargement was classified as grade 2 in four (12.5%), grade 3 in 17 (53%) and grade 4 in 11 (34.4%).

Dysmorphogenesis was diagnosed in 12 (37.5%) of the children. There were eight girls and four boys, giving a female to male ratio of 2:1. Their ages ranged from 6 to 14 years (mean 11.8). The consanguinity rate was 58%. Eight gave a family history of goitre and in three of these siblings were affected. Goitre was grade 2 in two cases (16.7%), grade 3 in seven and grade 4 in three. Enlargement was generalized and symmetrical in all of them, except in a 10-year-old girl who had multinodular goitre. The results of audiometry and BAER tests on all these children were found to be normal, except in the case of one 3-year-old

boy who was found to be deaf and was labelled a possible case of Pendred's syndrome. In the latter case, there was a 40% discharge rate. Eight of the children were hypothyroid and four were euthyroid. All were negative for thyroid autoantibodies and there was no history of exposure to iodine.

The prevalence of Hashimoto's thyroiditis in the study population was 34.4% with a female to male ratio of 4.5:1. Their ages ranged from 6 to 14 years (mean 11.8). Five came from central Saudi Arabia and five from the south-west and one from the north. Three had a positive family history of autoimmune thyroiditis. One child had Down syndrome. The goitrous enlargement was grade 2 in two, grade 3 in five and grade 4 in four children. Two of the latter had multinodular goitre. Five children were positive for antimicrosomal antibodies, one for antithyroglobulin antibodies, and five were positive for both. All had an antibody titre of $> 1:80$, except one who had a titre of 1:40. Thyroid functions showed evidence of primary hypothyroidism in eight and three were euthyroid. Four of the hypothyroid group, including the one with Down syndrome, had clinical signs and symptoms of hypothyroidism. An attempt to discontinue thyroxine in three of the hypothyroid group after 2-3 years of therapy was unsuccessful.

Graves' disease was diagnosed in four children. There were three boys and one girl, giving a ratio of 3:1. Their ages ranged from 5 to 11 years (mean 8). The 5-year-old had Down syndrome. All had exophthalmosy and two had positive thyroid-stimulating antibodies. All were treated medically initially. One eventually required thyroidectomy. The one with Down syndrome went into spontaneous remission after 4 years of medical treatment.

The children with simple goitre were all girls

with ages ranging from 6.5 to 11 years (mean 8.75). Two had diffuse symmetrical grade 3 enlargement of the gland and one had grade 4 asymmetrical enlargement (right > left). In this case, the thyroid scan was normal and a needle biopsy was suggestive of colloid goitre.

One child was found to have iodine deficiency. This 11-year-old Saudi boy from southern Saudi Arabia was referred with goitre of 30 months duration. He was found to have a grade 4 multinodular goitre and was both clinically and biochemically hypothyroid (free T4 6 (8.5–19.0 pmol/l), TSH 42 (0.3–3.8 mIU/l)). His thyroid antibodies, tested twice, were negative. Thyroid uptake showed increased uptake in the right lobe with multiple cold areas in the left and right lower lobes. Ultrasonography showed two cystic lesions in the left lobe. On aspiration, there was haemorrhagic fluid and no malignant cells were found. A potassium perchlorate discharge test showed >30% discharge. A urine sample for iodine showed low excretion (<9 µg/dl). There was no history of goitrogen intake. In his area of origin, people use non-iodized salt known as Sasa and apparently there was a history of many people in the village having goitre. He was initially treated with thyroxine and the goitre showed marked regression. He was later supplemented with iodide after the urinary iodine result had been received.

One child had cervical tuberculosis simulating a goitre. The details of this case have been published elsewhere.⁷

Discussion

The aetiology of childhood goitre varies in different countries and populations.^{1–4} Autoimmune lymphocytic thyroiditis has been reported to be the most common cause of thyromegaly during childhood in non-endemic goitre regions of the world. The present study has demonstrated a higher prevalence of goitre among females, as has been reported previously.^{1–4,8} In this study, dyshormonogenesis was the commonest cause of goitre whereas it

was very rare in other series (Table II). Dyshormonogenesis is an autosomal recessive disorder and it is not surprising to find a high incidence in a country where the consanguinity rate varies from 50 to 80%.⁹ Recently published figures on a Saudi nationwide neonatal hypothyroidism screening programme show that thyroid tissue was present in eight of 15 hypothyroid cases, and seven of these were proven to have dyshormonogenesis.⁹ Among 22 Saudi children diagnosed post-neonatally as hypothyroid, 16 had radionuclear studies and ten were found to have dyshormonogenesis.¹⁰ The best definitive test for the diagnosis of dyshormonogenesis is done by tissue analysis for enzymatic levels, but this facility was not available to us and current opinion is that such invasive methods should not be used, except for theoretical or pure research purposes.¹¹ The potassium perchlorate test is a sensitive but non-specific test for dyshormonogenesis. Positive results can occur in patients with iodide-induced goitre and after administration of goitrogens, and sometimes with Hashimoto's thyroiditis.^{11,12} All these were excluded in our patients.

Pendred's syndrome should be considered in any child with goitre, a positive perchlorate discharge test and deafness.¹³ Deafness with goitre and a positive perchlorate test can also occur in neurological endemic cretinism, and the discharge was 40% in our case. However, the discharge in endemic cretinism cases is almost 100%.¹³ Moreover, our case was otherwise neurologically normal and came from Riyadh city from where iodine deficiency has not previously been reported.

The second commonest cause of goitre in our study was autoimmune thyroiditis. Our figures are similar to those published from the United States¹ but higher than those reported from Croatia⁴ and Hong Kong⁵ (Table II). In one study from Saudi Arabia, antithyroid antibodies were detected in 8.1% of diabetic children under 12 years of age and in none of the control groups.¹⁴ Hashimoto's thyroiditis was found to be the cause of primary hypothyroidism in 9% of children below the age of 9 years diagnosed in Saudi Arabia.¹⁰ In a recent

TABLE II. Aetiology of childhood goitre: literature comparison (%)

	USA (1)	Hong Kong (3)	Croatia (4)	Saudi Arabia (SFH) This study
Simple goitre	14	34.5	82.9	9.4
Hashimoto's thyroiditis	33	2.4	12.5	34.4
Grave's disease	25	58.3	2.6	12.5
Dyshormonogenesis	7	—	—	37.5
Iodide deficiency	2	—	—	3.1
Thyroid tumours (adenoma + cancer)	7.1	1.2	1.3	—
Thyroid cyst	2	1.2	0.7	—
Others	9.9	0.4	0.7	3.1

survey of 1136 school children aged 11 to 21 years from south-west Saudi Arabia, 14.3% were positive for antithyroid antibodies.¹⁵ In Saudi Arabia, as elsewhere,^{1,3} the incidence of positive antibodies and Hashimoto's thyroiditis tends to increase with age. In addition to age, we suggest that this high incidence of antibodies in this tropical part of Saudi Arabia may be partially related to some environmental factors.

The incidence of Graves' disease in childhood is not unknown, but it is uncommon and has been reported to account for only 1–5% of cases seen in most thyroid clinics.^{16–18} In this study, Graves' disease accounted for 12.5% of cases. Our figures are lower than those reported from Hong Kong³ and the United States¹ but higher than those from Croatia⁴ (Table II). Unlike most other series,^{1–3} most of our patients were males. It is well known that children with Down syndrome are more likely than normal children to develop autoimmune thyroid disorders.⁵ In addition to one case of Down syndrome with Hashimoto's thyroiditis, one other of our Down patients had Graves' disease. Our experience of thyroid disorders among Saudi children with Down syndrome has been published elsewhere.¹⁹

The prevalence of simple goitre among children varies from 1 to 6%.^{20–23} As shown in Table II, the prevalence among those presenting with goitre in non-iodine-deficient areas varies from 14 to 82.9%. We found a low prevalence compared with those studies. This

is perhaps because we were dealing with a relatively younger age group: it is well known that the incidence of simple goitre tends to increase with age, particularly during puberty.⁸ The disease is said to follow an autosomal inheritance with a greater incidence in females.² All our patients were females. It has been suggested that many of these patients have thyroid growth-stimulating immunoglobulins.²⁴

Only one of our patients was thought to have iodine deficiency: a single urine specimen was analyzed for iodine content. Single urine specimens can be used to diagnose iodine deficiency,^{11,25} but perhaps we should have repeated the test to confirm our finding and should have offered iodine rather than thyroxine to support our diagnosis. However, the patient's goitre regressed on thyroxine (while we were awaiting the urinary iodide result) and we continued this treatment. He was later supplemented with iodine. In no series on hypothyroidism published from Saudi Arabia has iodine deficiency been documented.¹⁰ In one study of 221 school children in Riyadh, the mean (SD) iodine excretion per gram creatinine was 209 μg (148.3), suggesting a sufficient iodine intake.²⁶ However, low iodide concentrations were found in samples of tap water and mineral water analyzed from different regions of the Kingdom and it was recommended that iodized salt be used in Saudi Arabia.²⁷ Our patient was mostly using non-iodized salt, known locally as Sasa. In one

study of school children in Riyadh, the prevalence of goitre was found to be 0.9%,²¹ whereas more than 15% of children from the mountainous city of Abha in the south-west of Saudi Arabia were found to have goitre.²⁸

In this series, five children (15.6%) had multinodular goitres. Two had Hashimoto's thyroiditis and one each dyshormonogenesis, iodide deficiency and tuberculosis. No adenoma or carcinoma was encountered. The incidence of thyroid tumours and carcinoma varies from one country to another and thyroid carcinoma is perhaps seen more frequently in the USA than in other countries. In four published series on thyroid malignancy in Saudi Arabia, no malignancy was encountered in any patient under 9 years of age.²⁹⁻³²

In summary, the frequency and pattern of thyroid disorders causing goitre in Saudi Arabian children are different from those reported from other parts of the world. Dyshormonogenesis is as common as Hashimoto's thyroiditis, possibly due to the high incidence of consanguineous marriages. Further studies are needed to look into the problem of iodine deficiency, particularly in the mountainous areas of south-west Saudi Arabia. We suggest also that further studies on larger numbers of children from different parts of the Kingdom should be conducted to determine the prevalence and aetiopathogenesis of goitre.

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References

- 1 Mahoney CP. Differential diagnosis of goitre. *Pediatr Clin North Am* 1987; 34:891-905.
- 2 Alter CA, Moshang T. Diagnostic dilemma: the goitre. *Pediatr Clin North Am* 1991; 38:567-78.
- 3 Wong GWX, Leung SSF, Kwok MMY, Oppenheimer SJ. Goitre in Southern Chinese children in Hong Kong. *Ann Trop Paediatr* 1995; 15:27-31.
- 4 Jaksi CJ, Dunic M, Filipovic B, Iue J, Cvijetic M, Gjuric G. Thyroid diseases in a school population with thyromegaly. *Arch Dis Child* 1994; 70:103-6.
- 5 Al Nuaim A, Sulaimani R, El Desouki M, Abdullah MA. Thyroid gland dyshormonogenesis, a report of five cases with a review of literature. *Ann Saudi Med* 1989; 9:287-90.
- 6 Dunn JT, Crutchfield HE, Gutekunst R, Dunn A. Two simple methods for measuring iodine in urine. *Thyroid* 1993; 3:119-23.
- 7 Abdullah MA, Saleem MS, Salih H, Hamid FA, Asaaf H. Tuberculous anterior neck mass simulating goitre. *Ann Trop Paediatr* 1996; 16:369-71.
- 8 Dallas JS, Foley TP. Thyromegaly. In: Lifshitz F, ed. *Pediatric Endocrinology*. New York: Marcel Dekker, 1996; 383-9.
- 9 Al Nuaim A, El Desouki M, Al Jurayyan N, et al. Neonatal screening for congenital hypothyroidism: incidence, imaging, feasibility, and difficulties of a nationwide program. *Ann Saudi Med* 1992; 12:129-34.
- 10 Al Jurayyan N, Abdullah MA, El Desouki MI, Al Habib SA, Al Nuaim AA. Childhood hypothyroidism in Saudi Arabia: a retrospective study. *Saudi Med J* 1992; 13:125-8.
- 11 Vanderschueren-Lodeweyck M. Thyroid function tests. In: Ranke MB, ed. *Functional endocrinologic diagnostics in children and adolescents*. Mannheim, Germany: J & J Verlag, 1992; 37-60.
- 12 Hughes IA. The thyroid. In: Hughes IA, ed. *Handbook of Endocrine Tests in Children*. Bristol: Wright, 1986; 62-73.
- 13 Ilum P, Denmark O, Kiaer HW, Hansen JH, Sondergaard G, Denmark N. Fifteen cases of Pendred's syndrome. *Arch Otolaryngol* 1972; 96:297-304.
- 14 Abdullah MA, Salman H, Bahakim H, Gad Al Rab MO, Halim K, Abanainy A. Antithyroid and other organ specific antibodies in Saudi Arab diabetic and normal children. *Diabetic Med* 1990; 7:50-2.
- 15 Sulaimani RA, Al Atas OS, El Desouki MI, Bissa MA, Al Nuaim A. Thyroid autoantibodies: high prevalence among school children and adolescents in Gizan, Saudi Arabia. *Saudi Med J* 1995; 16:287-90.
- 16 Saxena KM, Crawford JD, Talbot B. Childhood thyrotoxicosis: a long term perspective. *Br Med J* 1964; 11:1153-8.
- 17 Johansen K, Khan M, Woodhouse NJY. High dose iodine 131 treatment of hyperthyroidism: experience at King Faisal Specialist Hospital and Research Centre. *Ann Saudi Med* 1988; 8:466-9.
- 18 Sulaimani RA, Mekki MO, Rohinivilasain VJ, Nyanissara S. Thyrotoxicosis: experience from the King Khalid University Hospital, Riyadh. *Ann Saudi Med* 1989; 9:455-7.

- 19 Abdullah MA, Salman H, Al Habib SA, Ghareeb A, Abanamy A. Antithyroid antibodies and thyroid dysfunction in Saudi children with Down syndrome. *Ann Saudi Med* 1994; 14:283-5.
- 20 Trowbridge FL, Matovinovic J, McLaren GD, Nichaman MZ. Iodine and goitre in children. *Pediatrics* 1975; 56:82-90.
- 21 Matovinovic J, Hayner NS, Epstein FH, Kjeisberg MQ. Goitre and other thyroid disease in Tecumseh, Michigan. *JAMA* 1965; 192:134-40.
- 22 Peden VH, Monteleone JA, Horvath VF. Incidence of goitre in an elementary school population. *J Pediatr* 1975; 86:816-17.
- 23 Murray TK. Prevalence of goitre in Canada (letter). *Am J Clin Nutr* 1977; 30:1573-4.
- 24 Van der Gaag RD, Drexhage HA, Wiersings WM, Brown RS. Further studies on thyroid growth stimulating immunoglobulins in euthyroid non-endemic goitre. *J Clin Endocrinol Metab* 1986; 60:972-6.
- 25 Frey HMM, Rosenlund B, Torgerson JP. Value of single urine specimens in estimation of 24 hours urine iodine excretion. *Acta Endocrinol (Kbh)* 1973; 72:287-92.
- 26 Stubbe P, Al Habib S, Thai H. Iodine excretion and goitre prevalence in Saudi Arabian children. *Saudi Med J* 1988; 9:476-80.
- 27 Sulaimani R, Al Attas O, El Desouki M, Eissa M, Al Nuaim AA, Al Sekait MA. Iodide concentration in Saudi waters: a cause of concern. *Ann Saudi Med* 1991; 11:655-7.
- 28 Sawaya WN, Tannous RI, Al Othaimen AI. Dietary survey of infants and preschool children in Saudi Arabia. Riyadh, Saudi Arabia: Ministry of Agriculture and Water Resources, Annual Report, 1985.
- 29 Al Tameem MM. The pattern of surgically treated thyroid disease in two general hospitals in Riyadh. *Saudi Med J* 1987; 8:61-6.
- 30 Mofti AB, Al Momen AA, Sulaimani SI, Jain GC, Asaaf HM. Experience with thyroid surgery in the Security Forces Hospital. *Saudi Med J* 1991; 12:504-6.
- 31 Kona S, Al Mohareb A. The surgery of goitre in Riyadh Armed Forces Hospital. *Saudi Med J* 1988; 9:617-21.
- 32 Al Tameem M. Thyroid malignancy in two general hospitals in Riyadh. *Saudi Med J* 1987; 8:67-72.