Congenital Hypothyroidism: Increased Incidence in Najran Province, Saudi Arabia

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Summary

Neonatal screening for congenital hypothyroidism using cord serum thyroid-stimulating hormone (TSH) was initiated in Najran health region in September 1990. A total of 30810 newborn infants were screened by April 1995. Of the 24 infants with abnormal thyroid function tests on recall, 22 had permanent primary congenital hypothyroidism (incidence; 1:1400) and in two male siblings transient congenital hypothyroidism (incidence; 1:15400) was proved on follow-up. There was a significantly higher incidence of dyshormonogenesis. Eight (57 per cent) of the 14 infants who were adequately studied thyroid scan revealed eutopic glands with increased ^{99m}Tc uptake, while thyroid ectopy and aplasia were present only in three (22 per cent) infants each. Furthermore, goiter was evident clinically in two other patients.

Introduction

Congenital hypothyroidism (CH) is one of the more common preventable causes of mental retardation. Its incidence worldwide is known to approximate one in 2500–5500 births.[1,2] Previous reports have shown that notable differences exist when the incidence and aetiology from various programmes are compared.[1–11]

Studies from different local programmes in Saudi Arabia have reported an incidence of one in 2500–3500.[12–15] The incidence in Najran health region is far high (one in 1400). We now present data from the regional screening programme in Najran. Najran province is situated in the South of Saudi Arabia (Fig. 1), and has a population of 350000, with an annual birth rate of 7500.[16]

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Materials and Methods

Screening for congenital hypothyroidism was introduced in Najran health region in September 1990 as part of the national screening programme. The entire region was being covered by January 1995. The programme utilized cord serum thyroid-stimulating hormone (TSH), supplemented with Serum Thyroxine (T4) if necessary. At the time of delivery, 4 cm^3 of cord blood was collected in a sterile tube from the placental side of the cord before delivering the placenta. Plasma was then separated immediately and kept at −20°C until the samples were delivered to Najran general hospital laboratory. During transportation, samples were kept in insulated containers.

TSH was assayed on single specimens using the Delfia Immunofluorescent (Pharmacia Diagnostic, Wallace Oy, Finland) technique. Total thyroxine (T4) (Delfia kits) was measured in the same specimen if TSH values > 30 mU/l. For quality control of TSH and T4 determinations at least three control sera (normal, low, and high levels) were analysed in each series.[13] The screening limits were TSH concentration more than 60 mU/l or 30–60 mU/l with a low T4 concentration of less than 80 nmol/l in the same blood screening sample.

All abnormal results were reported to the regional Co-ordinator (FS). Subsequently, the suspected cases were recalled for further evaluation and confirma-

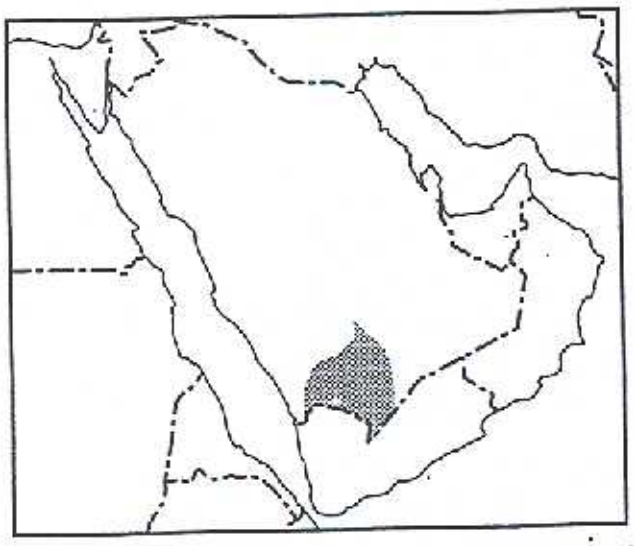

FIG. 1. Map of Saudi Arabia showing the location of Najran province.

tion. Appropriate clinical and diagnostic investigations were obtained. Thyroid scan was performed, when feasible, using sodium pertechnetate ^{99m}Tc. Perchlorate discharge test (PDT) was also performed in patients with suspected dyshormonogenesis following standard procedure.[17]

Confirmed cases were initially started on L-thyroxine 10–15 μg/kg/day, which was adjusted, thereafter, based on clinical and biochemical findings as recommended by the American Academy of Pediatrics.[1]

The diagnosis of primary congenital hypothyroidism was established in these infants on the basis of high TSH and low T4 levels on recall. The transient character of the hypothyroidism was evident by persistently normal TSH and T4 levels on follow-up, while being off therapy, in patients with normally located thyroid glands.

Results

A total of 30 810 newborn infants were screened during the period September 1990 to April 1995. Of those, 95 infants [TSH > 60 mU/l-(n = 31), and TSH 30-60 mU/l with T4 < 80 nmol/l-(n = 64)] had abnormal results and required retesting (recall rate: 0.3 per cent). Recall was not possible in four infants, with TSH values between 30 and 60 mU/l, due to either neonatal deaths (three infants), or lack of correct address (one infant).

Primary congenital hypothyroidism was confirmed in 24 infants; in two male siblings the abnormalities were transient. The remaining 22 (13 males and nine females) were from 20 families. A significantly high incidence of dyshormonogenesis among this group was observed. Thyroid scans were performed in 14 infants. The gland was athyreotic in three, ectopic in three, and eutopic with increased ^{99m}Tc uptake in eight. The perchlorate discharge test was performed in five of the eutopics and was positive. Furthermore, goiter was evident clinically in two other patients.

Seventeen (85 per cent) of the couples were consanguinous, and a family history of thyroid disorder was present in five families, either in a sibling (n = 2) or in a relative (n = 3). The mean age at the time of recall was 11 days (range 5–20) and that for start of therapy was 15 days (range 6–27). The physical and psychomotor development of these infants were normal, on increasing doses of L-thyroxine, throughout the follow-up period.

Table 1 summarizes the clinical and diagnostic data of the two male siblings with transient hypothyroidism. The parents were consanguinous and had no history of thyroid dysfunctions. The pregnancies had been normal and the babies were delivered at term. The mother did not receive any medication containing iodine or anti-thyroid drugs, and her urinary iodine was normal (17.4 μg/dl). She had no goiter or signs of hyper or hypothyroidism. Thyroid microsomal and thyroglobulin (haemagglutination method) antibodies were not detected either in the mother's or her baby's (sibling 2) serum. In a follow-up period of 3½ and 2 years following discontinuation of therapy, they continued to have normal growth and thyroid functions.

Discussion

The incidence of permanent congenital hypothyroidism diagnosed by routine neonatal screening in Najran health region was found to be one in 1400 newborn infants, a figure far higher than that reported from other regions in Saudi Arabia,[12–15] and that reported worldwide.[1–11] Recessively inherited enzyme defects in the synthesis of thyroxine account for the majority of our patients. This is probably due to the high rate of consanguinity among our group. Eighty-five per cent of our families were consanguinous. Saedi-Wong *et al.*[18] had reported a high rate (55 per cent) of consanguinous mating among Saudi Arabian population. Furthermore, Al-Jurayyan *et al.*[19] had shown in a retrospective study at a major referral hospital in Riyadh, Saudi Arabia, a significant correlation between consanguinity and thyroid gland dyshormonogenesis.

Of interest, is the finding of two full-term male siblings with transient hypothyroidism. Transient hypothyroidism has been reported in infants after exposure to antithyroid drugs or iodine-containing contrast agents during fetal life.[20,21] The mother did not receive any drug during pregnancy. Also, a higher frequency of transient hypothyroidism has been reported from areas of iodine deficiency.[22] The mother's urinary iodine and that for the babies were normal. Furthermore, Al Nuaim *et al.* (personal communication) have shown normal urinary iodine excretion in Najran's population. No antibodies were

TABLE 1
Clinical and diagnostic data in infants with transient congenital hypothyroidism

		Screening	Confirmation		Age	Clinical presentation	99mTc scan and uptake (%)	PD (%)	Urinary iodine (μg/dl)
		TSH (mU/l)	T4 (nmol/l)	TSH (mU/l)	T4 (nmol/l)				
Sibling 1	On recall	336	48	481	61	8 days	Goiter, umbilical hernia ND	ND	ND
	Off therapy	—	—	1.6	173	4 months	Normal Normal position 2%	ND	9.7
Sibling 2	On recall	123	59	437	27	21 days	Goiter, constipation, prolonged neonatal jaundice Normal position enlarged, 20%	63%	12.7
	Off therapy	—	—	2.1	148	12 months	Normal Normal position 1.6%	7%	ND

ND, not done; PD, perchlorate discharge.

detected in either the mother's nor her baby's (sibling 2) serum; therefore, the transient hypothyroidism was unlikely to have been caused by thyroiditis, in as much, a normally located thyroid gland with increased ^{99m}Tc uptake will exclude the possibility of maternal thyrotrophin binding inhibitory immunoglobulin.[23] Thyroid scan and perchlorate discharge test results in sibling 2 were suggestive of transient organification defect. This mechanism was first suggested by Delange *et al.*,[24] and later supported by Nose *et al.*[25] Based on computer search and, to the best of our knowledge, this is the first report on the familial pattern of the condition.

Finally, although it is important that a larger size of infants need to be screened and more information on the aetiology of the affected infants to be obtained, yet the current background information will be critical for appropriate genetic counselling in this society.

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