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# Neonatal screening for congenital hypothyroidism in Saudi Arabia: results of screening the first 1 million newborns

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**Abstract**

*Introduction*: Since the initiation of pilot screening programs to detect congenital hypothyroidism (CH) in 1972, newborn screening has become routine in the developed world. A national screening program for CH was established in Saudi Arabia in November, 1989. *Methods*: The program utilizes cord serum thyroid stimulating hormone (TSH), tested by the Delfia method, supplemented when necessary with thyroxine (T4) assay, also by the Delfia method. TSH values above 60 mU/l alone were considered suggestive of CH and initiated recall of the infant. TSH values of 30–60 mU/l initiated T4 measurement. If the latter was below 80 nmol/l, the infant was also recalled. *Results*: Between November 1989 and April 1995, a total of 1 007 350 infants were screened. The mean recall rate was 0.18% (range 0.05–0.3%). Of those, 306 infants were confirmed to have CH, indicating an incidence for CH in Saudi Arabia of 1:3292. However, a regional variation in incidence was noted. Of all the infants with congenital hypothyroidism who were adequately studied, 47.5% were found to have ectopic thyroid glands, 31.7% eutopic glands with increased $^{99m}$Tc uptake and 20.8% athyreotic. The mean age at the time of recall was 19.4 days (range 2–130). The average cost of screening was US $3.20 per specimen. *Discussion*: Several of the organizational and

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administrative difficulties which were encountered during the operation were discussed and solved at regional levels and during the annual general meetings.

*Keywords:* Neonatal screening; Congenital hypothyroidism; Saudi Arabia

## 1. Introduction

Since the initiation of pilot screening programs to detect congenital hypothyroidism (CH) in Quebec and Pittsburgh in 1972, newborn screening has become routine in the United States, Canada, Western Europe, Japan, Australia and New Zealand, and is under development in Eastern Europe, South America, Asia and Africa. It is estimated that 10–12 million infants are screened yearly with an incidence rate of 1 in 2500–5500 [1–6].

In Saudi Arabia, with a rapidly advancing health care system, neonatal screening for metabolic disorders has become a necessity. In light of the results of the local studies [7,8] and its pilot study [9], which showed a high incidence of CH, the Ministry of Health in collaboration with the College of Medicine of King Saud University established in 1989 an advisory committee for neonatal screening for metabolic disorders, with the main objective of promoting and establishing regional screening centers and supervising the quality of service provided [9].

We report here on the organization of the national program for neonatal screening for congenital hypothyroidism and present the preliminary results of screening the first 1 million newborns.

## 2. Materials and methods

### 2.1. Program organization

The advisory committee established an ad hoc committee (central committee) to formulate recommendations regarding neonatal screening for congenital hypothyroidism. Subsequently, regional screening programs were established in the different health regions (Fig. 1) which were equipped and supervised by local regional committees and consisted of a pediatrician, laboratory technician, administrator and social worker. Scientific and technical back-up were made available to all regions through the central committee.

Orientation lectures and scientific books were delivered to health care providers while the public was made aware of the screening through mass media such as local radio, television, newspapers and special pamphlets and posters. Reports on the progress of the regional programs are sent monthly to the central committee. Organizational and administrative difficulties are discussed periodically in annual general meetings.

### 2.2. Screening protocol

Considering the obstetric practice in Saudi Arabia where ~95% of mothers are delivered in hospitals, but with the majority being discharged within 24 h, the program utilizes umbilical cord serum with thyroid stimulating hormone (TSH) so as to achieve the maximum diagnostic benefits. At the time of delivery, 4 ml of cord blood is collected in a sterile tube from the placental side of the cord before delivery of the placenta. Serum is separated immediately and kept at −20°C until the samples are delivered to the Regional Central Laboratory. During transportation samples are kept in insulated containers.

TSH is assayed on single specimens using the Delfia Immunofluorescent (Pharmacia Diagnostic, Wallac Oy, Finland). Total thyroxine (T4) is measured using Delfia kits. For quality control of TSH and T4 determinations, at least three control sera (normal, low and high levels) are analyzed in each series [9,10].

Based on available data in the literature and the results of our pilot study [3,4,7,9–11] TSH concentration of more than 60 mU/l per se are considered suggestive of CH and warrant examination of the infant and repeat testing (see below). Cord serum TSH values of 30–60 mU/l initiate testing cord serum for T4.

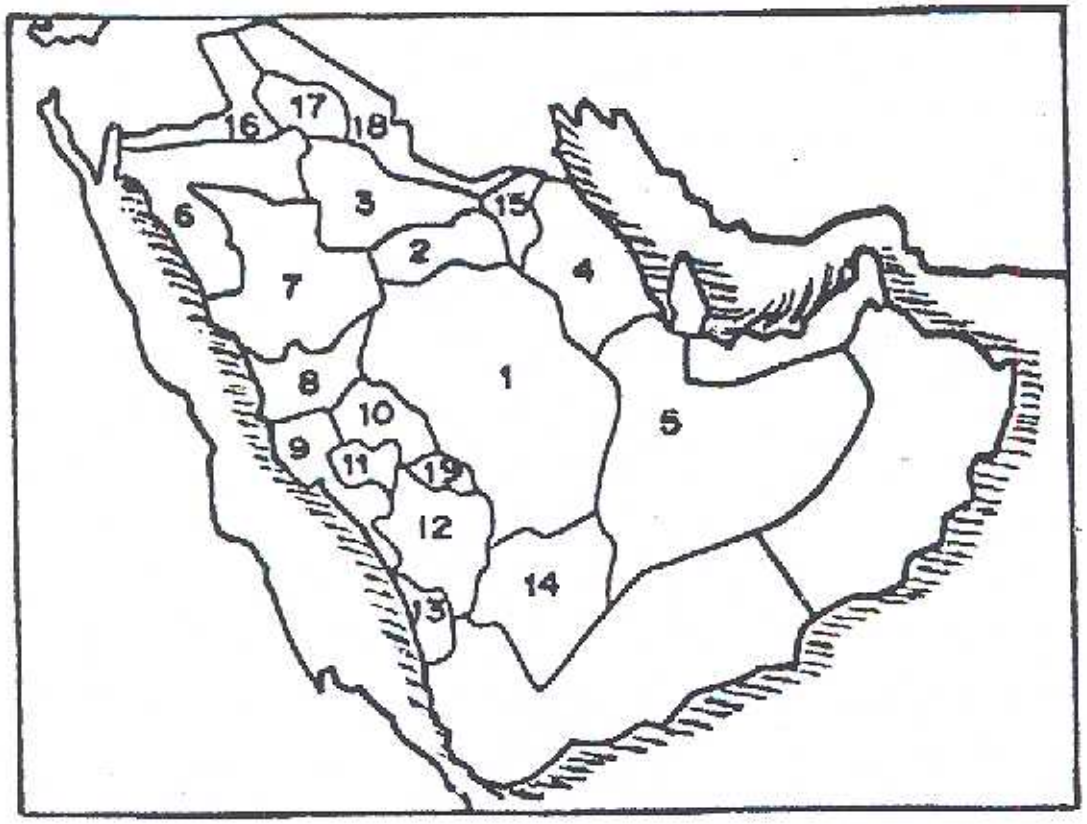


Fig. 1. Map of Saudi Arabia showing the different health regions: 1, Riyadh; 2, Qassim; 3, Hail; 4, Dammam; 5, Hassa; 6, Tabuk; 7, Madina; 8, Makkah; 9, Jeddah; 10, Taif; 11, Baha; 12, Assir; 13, Jizan; 14, Najran; 15, Hafer Al-Batin; 16, Qurayat; 17, Jouf; 18, Arar; 19, Bisha.

Those with T4 less than 80 nmol/l are also considered suggestive of CH and warrant recall of the infant. Cord serum TSH below 30 mU/l is considered normal. The quality control of the regional screening programs are done via lyphocheck immunoassay control serum by Biorad, California, USA.

### 2.3. Confirmation and further diagnostic evaluation and follow-up

After notification of a suspected case, the pediatrician will call the family for confirmation (repeat TSH and T4). At the time of diagnosis, clinical data are obtained which include: sex, age, nationality, consanguinity, family history of thyroid disorders, drug or irradiation during pregnancy, and symptoms and signs of hypothyroidism. Thyroid scan, to identify the etiology, was performed when feasible using sodium pertechnetate ($^{99m}$TC). Perchlorate discharge test was performed in patients with suspected dyshormonogenesis following standard procedure [12].

Infants confirmed with CH were treated initially with L-thyroxine 10–15 μg/kg/day, which was adjusted thereafter based on clinical and biochemical findings as recommended [6].

## 3. Results

Between November 1989 and April 1995, a total of 1 007 350 newborn infants were screened. The mean recall rate was 0.18% (range 0.05–0.3%), and the average cost of screening per specimen was US $3.20. Of those, 306 infants were confirmed to have CH, indicating an overall incidence of 1:3292. In 108 newborn infants, confirmation was not possible due to neonatal death (51 cases), lack of correct address or telephone number (49 cases), or travel outside the country (8 cases). Of these, 47 infants had cord TSH values greater than 60 mU/l and, 61 was TSH 30–60 mU/l with T4 values of less than 80 nmol/l. Some of these cases could represent true cases of congenital hypothyroidism. The general rate of death at birth in the country is 17.8 per 1000 live births [13].

Table 1 summarizes the numbers of infants screened and the numbers of infants confirmed to have CH in the different regions. A regional variation in the incidence was observed, highest in Najran and Bisha regions (1 in 1400 infants).

Table 2 summarizes the results of TSH and T4 in cord screening and at the time of recall, which indicates that an elevated TSH is the most sensitive test for diagnosis of CH. Some infants with ectopic thyroid or dyshormonogenesis have enough residual thyroid tissue to maintain T4 values within the normal range, either in the cord or recall samples. $^{99m}$Tc thyroid scan was performed in 183 infants. The gland was ectopic in 87 (47.5%), eutopic with increased uptake in 58 (31.7%) and athyreotic in 38 (20.8%). The age at recall varied considerably among regions with the mean being 19.4 days (range 2–130). In 238 (78%) infants the recall was within 3 weeks.

Table 1
Incidence of confirmed congenital hypothyroidism by the regional screening programs

| | Region | Total no. of newborns screened | No. of confirmed cases* | Incidence |
|---|---|---|---|---|
| 1 | Riyadh | 283 647 | 83 | 1:3417 |
| 2 | Qassim | 75 024 | 21 | 1:3573 |
| 3 | Hail | 32 750 | 5 | 1:6550 |
| 4 | Dammam | 65 523 | 20 | 1:3276 |
| 5 | Hassa | 57 176 | 21 | 1:2723 |
| 6 | Tabuk | 31 431 | 10 | 1:3143 |
| 7 | Madina | 82 371 | 28 | 1:2942 |
| 8 | Makkah | 75 874 | 25 | 1:3035 |
| 9 | Jeddah | 40 659 | 10 | 1:4066 |
| 10 | Taif | 55 404 | 20 | 1:2770 |
| 11 | Baha | 23 128 | 3 | 1:7709 |
| 12 | Assir | 65 774 | 16 | 1:4110 |
| 13 | Jizan | 38 303 | 10 | 1:3830 |
| 14 | Najran | 30 810 | 22 | 1:1400 |
| 15 | Hafer-Al-Batin | 15 977 | 4 | 1:3994 |
| 16 | Qurayat | 9360 | 2 | 1:4680 |
| 17 | Jouf | 7920 | 1 | 1:7920 |
| 18 | Arar | 12 095 | 2 | 1:6047 |
| 19 | Bisha | 4124 | 3 | 1:1374 |
| | Total | 1 007 350 | 306 | 1:3292 |

*Figures exclude those infants in whom confirmation was not possible.

## 4. Discussion

Neonatal screening programs for congenital hypothyroidism (CH), which have been in effect for more than two decades in most of the developed countries, are lacking in developing countries [5,6]. In Saudi Arabia, neonatal screening for metabolic disorders is a necessity that has become a reality within the rapidly advancing health care system. In this, the Ministry of Health has established the nationwide screening program for CH that has continued for over 5 years [9]. Considering the geographical distribution and wide scatter of the population, the program was subdivided into smaller regional programs which are fully supported through a central committee. As the local custom of early discharge of infants and

Table 2
TSH and T4 values of cord serum (screening) and venous serum (recall) specimens in confirmed cases of congenital hypothyroidism; mean ± S.D. (range)

| Cord blood (screening) | | Venous blood (recall) | |
|---|---|---|---|
| TSH mU/l (Normal <60) | T4 nmol/l (Normal 80–200) | TSH mU/l (Normal <10) | T4 nmol/l (Normal 80–180) |
| 407 ± 138 (53–1070) | 64 ± 13.8 (14–153) | 487 ± 189 (59–1060) | 51.3 ± 48.6 (10–220) |

their mothers presents a logistic difficulty, the program utilizes cord blood for screening. Although cord blood samples have ensured that many infants did not escape the screening process for CH, this sample is not suitable for screening for metabolic disorders such as phenylketonuria and galactosaemia. However, these disorders are less frequent in Saudi Arabia than elsewhere. No single case of phenylketonuria was detected by Abu Osba et al. [8] during screening of more than 70 000 newborn infants in ARAMCO program.

The incidence of confirmed infants with CH in our population, 1 in 3292, is comparable to what has been reported by Abu Osba et al. [8] from the Eastern region of Saudi Arabia and consistent with other reports from Europe and North America [1–6]. If we consider infants with positive cord screening and in whom confirmation was not possible, however, the incidence might be even higher. This is in support of our previous pilot study [9], and similar to that reported by Bacchus et al. [7] from another local study from Riyadh-Al Kharj Military hospital program. A regional variation in the incidence was observed, being the highest in Najran and Bisha regions with a frequency of 1:1400 infants. This could be explained in part by the regional variation in the numbers of infants in whom confirmation was not possible. It is not likely to be explained on the basis of iodine deficiency. Stubbe et al. [14], have indicated that Saudi children in Riyadh region have normal urinary iodine excretion rates and this has been ascertained as well in other regions (Al Nuaim et al., unpublished data). The high frequency might be due to a genetic element influenced by consanguinity [1,5,15–18]. Saedi-Wong et al. [19] have shown a high incidence of consanguineous matings in the Saudi Arabian population and thyroid gland dyshormonogenesis was observed in the majority of infants from Najran province [20]. Furthermore, dyshormonogenesis was suggested in more than 30% of infants in whom thyroid scanning was performed [12]. This high incidence of dyshormonogenesis is in contrast to the findings in other countries [1,21].

Our protocol produced an acceptable recall rate and proved to be cost effective [1,2,22]. The age at recall varied considerably among regions, and reflects the importance of the availability of communication means such as telephones and clear addresses. An appreciable proportion of those infants in whom recall was either impossible or delayed lack such means. More efforts are needed to improve communication both at the medical and public levels. Finally, our experience indicates that the successful implementation of any screening program depends not only on efficient and comprehensive collection of specimens, transport and laboratory processing but also on continuous public awareness and availability of access to the patients and parents for prompt recall for further testing or therapy as indicated.

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