Congenital hypothyroidism in Saudi children

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Congenital hypothyroidism (CHT) is one of the most common preventable causes of mental retardation in children. Diagnosis based on clinical features is usually difficult and clinical features are often lacking at birth and for the first few weeks or months of life. Studies based on clinical diagnosis have demonstrated that less than 50% of CHT cases are diagnosed within the first three months and only some two-thirds by the age of one year.[1,2] However, since the introduction of the first neonatal screening (Quebec and Pittsburgh) in 1974,[3] incidence of CHT now appears higher, with worldwide variation in incidence between 1 in 2500 and 1 in 5500.[4]

In the Saudi Arabian population, a report from Najran (a southern province of the country) reported an incidence of 1 in 1400,[5] which is higher than in Riyadh[6] or other parts of the world. Here, we assess the incidence of CHT during 2000 and 2001 for the population of Riyadh, and compare it with that reported earlier by us in a study using a blood spot technique.[7]

It is hospital policy to screen the cord blood of every newborn for thyroid stimulating hormone (TSH) level. King Fahad National Guard hospital is a tertiary care hospital that serves mainly the families of National Guard recruits who live in the Riyadh area. All babies delivered in the hospital are Saudi nationals, mainly from the central region of Saudi Arabia. Results for 2000 and 2001 were analysed to assess the normal range for cord blood TSH and to calculate the incidence of CHT in this Saudi population.

Cord blood samples were collected in serum-separated tubes (Becton Dickinson), transferred to the laboratory, centrifuged and the serum stored at –20°C. TSH and free T4 levels were measured using an automated chemiluminescence immunoassay analyser system (ACS-180SE; Bayer Diagnostics, USA). This is a third-generation immunoassay system that uses constant amounts of two antibodies. The first antibody (in the reagent) is a monoclonal mouse anti-TSH antibody labelled with acridinium ester. The second antibody (in the solid phase) is a polyclonal sheep anti-TSH antibody, coupled covalently to paramagnetic particles.

Babies with high cord blood TSH levels above the cut-off value (>30 mIU/L) were recalled within a week and a venous blood sample was collected. Venous blood samples were assayed for TSH and free T4 to confirm the diagnosis of CHT and confirmed cases were given a thyroid scan. Venous TSH and free T4 assays were used as gold standard tests for determination of thyroid status and in treatment follow-up.

Table 1 summarises the results of cord blood TSH in children born during 2000 and 2001, and the number with values >30 mIU/L is relatively high (63 and 66, respectively). However, when further tests were carried out on these infants, only three in each year were diagnosed with CHT. All confirmed cases showed a high cord blood TSH level (Table 2). There were 6845 newborns in total during the year 2000 and 6827 in 2001, which gave an incidence of 1 in 2282 and 1 in 2276, respectively, and an overall incidence of 1 in 2279.

Using a cut-off value of 60 mIU/L produced a smaller number of false positives (11) and gave a specificity of 99.2% and sensitivity of 100%. Using 30 mIU/L as the cut off value resulted in 140 false-positive cases; however, 100% sensitivity and 98.9% specificity were not significantly different from those achieved using the higher cut-off value.

Free T4 estimation was performed when the cord blood TSH level was above the cut-off value. For those with cord blood TSH >30 mIU/L, mean free T4 was 13.5 pmol/L and mean cord blood TSH was 58.1 mIU/L (Table 2). Babies with borderline TSH values were followed up in clinic. The cut-off value of 30 mIU/L was determined from a local study conducted by Al-Jurayyan *et al*.[6]

The incidence of CHT in the Riyadh area is similar to that reported in other countries but lower than that reported in Najran, a southern province of Saudi Arabia, where the incidence is 1 in 1400. Increased frequency (85%) of consanguineous marriage compared with that in the rest of the Kingdom (55%) was suggested as a possible explanation for this,[5] with recessive inheritance of enzyme defects in the synthesis of thyroxine suggested as the cause of this high incidence in Najran.[5] Reports from other regions of Saudi Arabia suggested CHT incidences of 1 in 2500 to 1 in 3500.[6] These figures are comparable with the worldwide incidence of CHT.[4]

The figures presented here are in agreement with those reported in a previous study from this hospital that looked at data obtained between 1983 and 1988,[7] using a blood spot total T4 radioimmunoassay. We believe that cord blood TSH is a simple and easy screening method; however, the high level of false-positive results and thus the number of babies that need to be recalled for further investigation are disadvantages of this approach.

Although more females than males are affected by CHT, it is interesting to note that cord blood TSH levels in males were higher (but not significantly so) than those in females. This could be due to biological factors such as birth weight but we do not have data to investigate this difference in the group at large.

The incidence of CHT in Thailand is reported to be 1 in 2949 live births.[8] In the 12 CHT cases reported over five years, cord blood TSH levels were found to be >50 mIU/L; therefore, the authors upgraded their cut-off from 30 to 40 mIU/L.

We believe that the high incidence of CHT in the Saudi population supports the need for a neonatal screening programme. However, although the six confirmed CHT cases in the present study had TSH levels >60 mIU/L, we would be wary of increasing the cut-off value from 30 to 60 mIU/L, as some false-negative cases might be missed. In addition, we found that sensitivity and specificity were comparable and therefore we will continue to use the lower cut-off value and collect more data to establish a more appropriate figure.

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Table 1. Cord blood TSH results

Year		Newborns	Median	Mean	TSH >30 (mIU/L)	TSH >60 (mIU/L)	Confirmed CHT*
2000	F	3320	5.85	7.21	28	5	2
	M	3525	6.40	7.80	35	3	1
	Total	6845	63	8	3		
2001	F	3336	5.60	7.11	21	6	2
	M	3491	6.30	8.11	45	3	1
	Total	6827	66	9	3		

* All confirmed cases had cord blood level >60 mIU/L.

Table 2. Cord blood and serum TSH levels and free T4 in confirmed congenital hypothyroidism cases

Case	Sex	Case Sex Cord blood TSH (mIU/L)	Serum TSH (mIU/L)	FREE T4 (pmol/L)
1	F	184.5	Not Available	10.9
2	F	325.5	151.4	6.4
3	M	651.5	703.5	4.99
4	M	354.7	88.2	11.05
5	F	131.0	47.7	11.12
6	F	751.3	135.7	4.38

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