

## Pilot Study on Neonatal Screening for Congenital Hypothyroidism in Iraq

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### Summary

**Background:** Neonatal screening for congenital hypothyroidism (CH) is an essential preventive public health program for early identification of disorders that can lead to potentially catastrophic health problems

**Objectives:** This is a pilot study conducted to determine the incidence of CH among infants born in two major maternity hospitals in Baghdad City and to build a model for nationwide screening program.

**Methods:** A prospective study on screening of all newborns was conducted in two major maternity hospitals in Baghdad, from 01.12.2001 - 31.12.2002. A total of 6949 neonates were screened for CH, cord blood samples were examined for serum TSH levels by immunofluorescent method (ELIZA) and reexamined for T4 using a cutoff sTSH value of 40 mIU/L.

**Results:** Three neonates were proved to have Congenital hypothyroidism (incidence of 1: 2275), forty eight (0.7%) neonates had sTSH > 40mIU/l. Females and neonates delivered by Cesarean sections and premature neonates had a higher predilection for hyperthyrotropinaemia.

**Conclusion:** The incidence of CH is notably approximate to the incidence of the disease in the nearby and surrounding countries and higher than other mountainous developing countries and much higher than the incidence of CH in Europe. The present study found that neonatal screening program can be handled in the hospitals and required further coordination to adopt a nationwide screening program which must be started in Iraq.

**Keywords:** Hypothyroidism; neonatal screening; thyrotropin, cord blood

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### Introduction

Neonatal screening is an essential preventive public health program for early identification of disorders that can lead to potentially catastrophic health problems (1). The purpose of neonatal screening programs is the commencement of treatment of selected patients within the first two weeks of life (2). The majority of European and Japanese programs conduct screening by means of primary sTSH measurement supplemented by T4 determination for those infants with elevated TSH value. Newer TSH assay techniques such as enzyme linked immunoassay offer the advantage of using non-radio labeled technique and greater sensitivity with the potential for better separation between normal and abnormal TSH concentration (3). The screening tests for congenital hypothyroidism (CH) appear to serve monitoring of iodine deficiency disorders, and prevent mental retardation in infants born with this condition in developing countries (4). The screening programs for CH showed differences between different countries in the detection of

organization and follow up of the screening program, CH being more common in developing countries than in developed countries. The vast majority of infants are now diagnosed after detection through screening programs using primary T4-backed TSH or primary TSH test (5).

This is a pilot study conducted to determine the incidence of CH among infants born in two major maternity hospitals in Baghdad City and to build a model for nationwide screening program

### Patients and methods

This is a prospective pilot study conducted in two major maternity hospitals in eastern Baghdad, Al-Habibiya Maternity Hospital and Ibn Al Bilty Maternity Hospital, between the 01.12.2001 and 31.12.2002.

A data sheet for each neonate was filled by a nurse including registry number, name of the mother, date of delivery, sex of the neonate, gestational age, type of delivery, and address of the family. The nurses in the delivery rooms and operative theater were trained on filling the data sheets and taking the cord blood samples, and supervised through frequent visit by the primary researcher. A total of 6949 neonates were screened for CH, using 5 ml of cord blood samples taken at birth by nurses trained for that purpose. The

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samples were centrifuged at the hospital laboratory and the serum was separated and stored in deep freeze temperature in the same laboratory. The samples were transferred to the central laboratory in the Center of Endocrinology and Diabetes, once weekly.

The serum samples were examined for serum TSH levels using immunofluorescent method (ELIZA). The TSH cutoff value for recall was 40 mIU/L. All the samples above this cutoff value were examined for free T4 (FT4). All values of TSH equal to or exceeding 40 mIU/L were recalled for TSH and FT4.

### Results:

Of the total 6949 neonates included in the study, 123 samples were excluded due to laboratory errors and / or mismanaged collection of the cord blood samples. This left 6826 neonates, who were considered eligible to be included in the study. There were 3570 males (52.3%) and 3256 females (47.7%), giving a male: female ratio of (1.1:1).

The recall value which was selected to conduct the other screening programs was taken as sTSH value of 40mIU/L. Forty eight (0.7%) neonates had sTSH > 40mIU/L, and only five neonates had cord blood sTSH >100mIU/L. Of the 48 newborns who had hyperthyrotropinaemia (sTSH >40 mIU/L), there were 32 females, and 16 males giving a female to male ratio of 2:1, Table (1).

Table (1): Sex Distribution of the screened neonates

Sex	Total No. (%)	Hyperthyrotropinaemic sTSH >40 mIU/L No. (%)
Female	3256 (47.7)	32 (66.7)
Males	3570 (52.3)	16 (33.3)
Total (100 %)	6826 (100)	48 (100)

All those neonates were re-examined for FT4, and had to be re-evaluated for sTSH and FT4. Three neonates were confirmed to have congenital hypothyroidism; all were full term females who were delivered normally. There were 1365 neonates delivered by Cesarean section (20%), none of whom was found to have CH. Table (2) shows the distribution of the neonates by the type of delivery and sTSH level.

Table (2): Distribution of the Neonates by the Type of delivery and sTSH level

Type of delivery	Number	sTSH >40IU/L No. (%)	sTSH <40IU/L No. (%)
Normal	5461 (100 %)	39 (0.7)	5422 (99.3)
Cesarean Section	1365 (100 %)	9 (0.6)	1356 (99.4)
Total	6826	48	6778

$X^2=0.0472$ ,  $df=1$ ,  $p (>0.05, NS)$

Among all the screened neonates fifty eight (0.9%) were delivered prematurely (before 37weeks of gestational age), one was found to have hyperthyrotropenaemia, Table (3).

Table (3): Distribution of Neonates delivered normally by Gestational age and sTSH level

Gestational age	Number of Newborns	Newborns with sTSH >40IU/L No. (%)
Full term => 37wks	5412	38 (0.7)
Premature < 37 wks	49	1 (2)
Total	5461	39

$X^2=1.6561$ ,  $df=1$ ,  $p (>0.05, NS)$

Of the neonates studied, 5412 were delivered normally and were full term (=>37 weeks gestation), 39 (0.7%) had sTSH >40IU/L. There were 49 (0.7%) premature newborns (<37 wks) delivered normally and 1 (2%) had TSH >40mIU. Table (3)

Table (4): Distribution of neonates delivered by Cesarean section by gestational age and sTSH level

Gestational age	Number of Newborns	Newborns with sTSH >40IU/L No. (%)
Full term => 37wks	1356	9 (0.66)
Premature < 37 wks	9	0
Total	1365	

Those who were delivered by caesarian section (CS) were 1365, of whom nine (0.66%) neonates had sTSH >40IU/L and none was premature. Table (4)

### Discussion

Screening programs for congenital hypothyroidism were carried in many countries with different designs. Many previous screening programs depended on collecting cord blood sample immediately after delivery (4, 6, 7, 8) claiming technical superiority of umbilical cord blood sample over heel prick blood sample (7). The trend in Iraq is to discharge the mother few hours after normal delivery so in the present study it was considered to be easier to obtain cord blood sample than to trace the newborns to their homes, which would require facilities, personnel, and additional costs.

Different opinions existed regarding the TSH cutoff value. Many workers considered TSH cutoff value of 30mIU/L (6, 7), while other workers started their studies using cutoff value of 30mIU/L then they discovered that it was more sensitive and more practical to use TSH value of 40mIU/L as a cutoff value that carried less false positive results (6, 9). Wu et al considered 20mIU/L as the standard TSH cutoff value (8).

The study showed higher recall value than other studies even if they had less or the same incidence of congenital hypothyroidism (10)

Controversy has persisted regarding the relative merits of primary T4 screening (5, 7, 11, 12) with follow up TSH measurement on samples with low T4 values versus primary TSH screening (3, 6, 8, 9, 13, 14, 15, 16). North American programs have tended to utilize primary T4 screening (9) whereas in Europe and Japan TSH screening is generally employed (3,

16,17). A comparative study in Poland, 1999 showed that primary T4 screening has similar sensitivity compared to TSH screening in heel prick sample in many screening programs for CH (2). However, another comparative study in Brazil described TSH screening as superior to primary T4 in neonatal thyroid screening for CH (18). In the present study TSH screening was preferred due to its sensitivity in the cord blood samples.

The incidence of CH in the present study, which was conducted in Baghdad city, might reflect the incidence of the condition in Iraq due to the wide representation of population of Iraq in Baghdad. The incidence of CH in this study was 1/2275 live birth. This incidence is notably approximate to the incidence of the disease in the nearby and surrounding countries (Oman, Saudi Arabia, Turkey and Palestine/west bank) (19, 20, 21). The incidence is higher than that reported in other developing countries like Thailand (6, 7). The incidence of CH in the present study is much lower than that in Pakistan (1/1000) (22). The incidence of CH in France (3/10,000) is lower than the present results (9). However, other parts of Europe have an incidence of CH similar to ours, such as Portugal (1/2500) and Estonia (1/2860) (5, 9).

This is probably a reflection of moderate iodine deficiency which is a nutritional problem in our country (23, 24).

The present study found that females had a higher pre-dilection for hyperthyrotropinaemia. Three neonates who were delivered normally were found to have CH. The study found that hyperthyrotropinaemia is higher ( $p > 0.05$ ) in neonates born by CS than those born by normal delivery (Table 2) and that is coincide with other studies (9, 10)

Significantly elevated levels of TSH (hyperthyrotropinaemia) could be found among preterm babies as compared to full term babies delivered normally unlike other studies (6, 14)

In conclusion the incidence of CH in the present study is similar to incidence in the nearby and developing countries as compared to developed countries probably because of iodine deficiency in the diet in Iraq and the delayed or inconsistent actions that was taken in the last 20 years because of the wars, sanctions and the political disturbances in the country(23, 24), also it might be related to consanguineous marriages so the problem needs further study to erase the causes.

This study might be used as a step for introducing a national screening program for CH in Iraq as it proved that can be conducted in hospitals following an intensive training course for doctors, nurses and laboratory personnel. From the above discussion it seemed logic to use cord blood samples at birth for its simplicity and convenience especially in hospital deliveries.

The study did not cover neonates delivered at home. Still we recommend to start the screening in selected hospitals in five governorates as it was planned for in Egypt (25) and then the screening can be expanded

according to the problems and successes to be national screening program covering hospital and home delivery neonates

The use of sTSH for primary screening and FT4 measurement for recall is preferable; also it is more cost effective and reasonable to use sTSH cutoff value of 40mIU/L for primary screening.

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