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Original Article

Newborn Screening for Congenital Hypothyroidism in a Public Sector Hospital

Farkhanda Ghafoor[1], Saima Naz Mohsin[1], Shafqat Mukhtar[2], Saira Younas[3], Waqar Hussain[2]
National Health Research Complex, Shaikh Zayed Medical Complex[1], Gynae Unit 1, Shaikh Zayed Hospital[2], Jinnah Hospital[3], Lahore.

Abstract

Background: Congenital hypothyroidism if left untreated results in growth failure, irreversible mental retardation, and cretinism. National neonatal screening programs are therefore, launched to diagnose congenital hypothyroidism and manage it timely.
Objectives: To screen new borns for congenital hypothyroidism in two public sector hospitals of Lahore.
Study type, settings and duration: Cross sectional descriptive study conducted at departments of Gynae/Obs & Pediatric Shaikh Zayed Hospital and Jinnah Hospital, Lahore from February 2010 to November 2011.
Subjects and Methods: Awareness brochures for congenital hypothyroidism were developed and attached with the antenatal card of each pregnant case attending antenatal clinic at Gynae/Obs OPD. Newborns who had stayed in hospital for more than 24 hour, and whose parents consented for heal prick were tested for blood spot thyroid-stimulating hormone. Results were reported within four days and thyroid-stimulating hormone ≥ 20mIU/L was taken as high value. Parents of those neonates who had high value were contacted to give a fresh sample for confirmation. Confirmed results were provided within next 4-5 days to the parents and treating pediatrician for appropriate treatment.
Results: A total of 1357 samples were screened using blood spot thyroid-stimulating hormone and out of these 1330 were normal (< 20mIU/L) while 27 had high levels (≥ 20mIU/L). These 27 neonates were further tested using confirmatory tests for serum thyroid-stimulating hormone, T3 & T4. After confirmatory tests only one case had congenital hypothyroidism who was referred for treatment. Three cases were suspected to have subclinical hypothyroidism and these were retested after six months which, picked another case of confirmed subclinical hypothyroidism who was referred for treatment. The incidence of congenital hypothyroidism was 2 out of 1357 cases.
Conclusion: The screening could pick 2 cases of hypothyroidism from a total of 1357 cases which is high when compared to global rates.
Policy message: Routine screening of neonates for thyroid disease can pick the disease early and thus prevent later complications.
Key words: Congenital hypothyroidism, neonatal screening, blood spot, thyroid-stimulating hormone (TSH).

Introduction

Congenital hypothyroidism (CH) is a congenital metabolic disorder in which infants are unable to produce sufficient amount of thyroid hormone (thyroxin or T4) which is necessary for their metabolism, growth and brain development[1]. This disorder if left untreated results in growth failure, irreversible mental retardation, and a variety of neuropsychological deficits and cretinism[2,3].

In 80-85% cases of congenital hypothyroidism, the thyroid gland is absent, abnormally located, or is small while, in remaining cases, a normal-sized or enlarged thyroid gland is present, but the production of thyroid hormones is decreased or absent[4].

Clinical diagnosis of hypothyroidism in neonates can be done in less than 5% cases[2] therefore, neonatal thyroid screening is a tool for its early detection and treatment[5-7].

The introduction of routine neonatal screening was started in many countries in 1970s and data from these countries shows that almost twice number of CH were picked when compared with countries where screening is not done[2].

In UK and USA around 25 babies are born with CH in every 100,000 births which is equivalent to one in 4000 births[8]. In Asia this ratio is 1:2000 births and in iodine deficient areas it is 1:1500 births[2]. In UK and USA, problem of CH is seen less common among newborns of African and African-American mothers compared to infants born to mothers of Indian, Pakistani and Bangladeshi origin[9]. An Indian study reported a 2.1 per 1000 (6/2872) incidence[10] which, is much higher than

Corresponding Author:
Farkhanda Ghafoor
National Health Research Complex
Shaikh Zayed Medical Complex
Lahore.
Email: fghafoor99@hotmail.com

1 in 1700 from other regions of India[11]. A study from Pakistan reported an incidence of 1 in 1000 newborns which is almost 4 times higher than that the West[12].

In many countries where screening was not done routinely, many children had CH disorder with moderate to profoundly mental retardation but recent prospective studies in these countries have demonstrated normal or near-normal intelligence in virtually all of those detected and treated early in life for CH[13,14]. Screening the newborn before hospital discharge, (more than 24 hrs after birth) or before transfusion, is the preferred time to diagnose these cases.

Newborn screening program once established will offer the opportunity to use the same infrastructure and specimens to detect other congenital disorders to improve health status of newborns in Pakistan.

Subjects and Methods

This cross sectional descriptive study was initially started at departments of obstetrics/ gynecology, pediatric, Shaikh Zayed Hospital Lahore and after 08 months, Gynae I unit, and department of pediatric Jinnah Hospital Lahore was also included. All the pregnant cases attending antenatal clinic of these hospitals were explained the importance of screening of hypothyroidism in neonates. Awareness brochures for the disease were developed and attached with antenatal card of each case attending antenatal clinic. After delivery, informed consent was taken from those who agreed to provide blood of neonate from heel using prick method. Heel was pricked after 24 hours of delivery but within 5 days. Two drops of blood were spotted on special filter paper which was marked with circles and attached to respective card with demographic information about parents, siblings and neonate. The filter papers were dried at room temperature for 3-4 hours. All cards were brought to NHRC laboratory and tested twice a week for TSH using radio-immunometric method. Quantitative results were calculated using muticalc programme attached to gamma counting system from NETRIA UK. All values ≥20mU/L were considered as high or hypothyroid and those <20mU/L were taken as normal.

Neonates having spot TSH levels ≥20mU/L were called back using recall strategy. Two ml of fresh venous blood was drawn from these cases, serum was separated and tested for TSH, T3, and T4 using ELISA method. The results were provided within next 4-5 days to parents and treating pediatrician for appropriate treatment. Newborns with grey area report (subclinical hypothyroidism) were contacted and retested in NHRC immunoassay lab after six months for confirmation of diagnosis.

The data was entered and analyzed using SPSS version 15.0. Tests for blood spot TSH level were reported using frequencies in different ranges. TSH, T3 and T4 levels were reported as mean for confirmed, suspected subclinical and euthyroid cases. Gender, gestational age, birth weight, consanguinity in parents, congenital anomalies and mother's thyroid status was also recorded, but was only reported for confirmed hypothyroid neonates.

Results

A total of 1357 neonates were screened for congenital hypothyroidism and of them 1330 had normal spot TSH < 20mIU/L (998 had TSH level < 10mIU/L, 243 had 10-15mIU/L and 89 had 16-20mIU/L). High levels ≥ 20 mIU/L were found in 27 samples who were suspected to have congenital hypothyroidism.

Table 1: Confirmational analysis of suspected newborns for congenital hypothyroidism.

Diagnosis	*N*	*Mean TSH mIU/L*	*Mean T3 nmol/L*	*Mean T4 nmol/L*
Confirmed Congenital Hypothyroidism	1	84.6	1.3	65
Suspected Subclinical Hypothyroidism	3	9.9	2.0	147
Euthyroid	23	3.0	1.7	141

Normal ranges TSH = 4 days after birth----- 1.0-3.9 mIU/L
2-20 weeks ---------- 1.7-9.1 mIU/L
T4 = 79-162 nmol/L, T3 = 1.5-3.3 nmol/L

Table 2: Demographic features of newborns diagnosed for congenital hypothyroidism.

Profile of Newborn	*Diagnosis*	
	Congenital Hypothyroid	*Subclinical Hypothyroid*
Gender	Female	Male
Premature/ Full term	Full term	Full term
Gestational Age	37 weeks 2 days	38 weeks 6 days
Birth Weight	3.6 Kg	2.1 Kg
Baby status at birth (Normal/Sick)	Normal	Normal
Congenital anomalies in siblings	No	No
Consanguinity in parents	No	No
Mother's thyroid status	Euthyroid	Euthyroid

Blood samples of these 27 neonates were confirmed using venous blood for total thyroid hormones i.e. serum TSH, T3 and T4 using ELISA. Twenty three neonates had normal TSH, T3 & T4 levels) and only 01 had high levels of TSH with low T3& T4 (congenital hypothyroidism) while, 03 were suspected to have subclinical hypothyroidism (High TSH. normal T3, T4). These 3 suspected neonates were followed for 6 months when these tests were repeated again, using ELISA. Two neonates had normal values while, the third one had subclinical hypothyroid. The overall incidence of congenital hypothyroidism therefore, was 2 in 1357

neonates (Table-1). Both cases were put on treatment by their pediatricians.

No association of congenital hypothyroid and subclinical hypothyroid was seen with gender, gestational age, birth weight, congenital anomalies in siblings, consanguinity in parents and mother's thyroid status (Table-2).

Discussion

The current study showed 02 in 1357 incidence of congenital hypothyroidism in neonates which, is higher than 1 in 1000 reported from Karachi[12].

In this study 27 cases had high TSH which, could be due to sub clinical hypothyroidism or iodine deficiency. Similar findings were reported by others[2,15]. Other reason could be screening after 24 hours, as the biological surge occurs shortly after birth, peaks at about 6–2 hours and diminishes over the next 24–48 hours[16]. The incidence of false positive results are high if the screening is done within 24-48 hours of life[17].

For a national newborn screening program it is beneficial to have false positive cases to ensure that no case is missed. All high TSH cases can be further confirmed by recall but if left undiagnosed these may go to irreversible mental and physical disabilities. With sensitive assay ideal recall rate is 1.0% which in this study was 1.98% probably due to being in the initial stages of establishing the neonatal screening program. A retrospective study carried out at Aga Khan University Hospital Karachi, reported 15% recall rate at 13 mIU/L, 5% at 20mIU/L and 2.3% at 25mIU/L respectively[18].

In this study female to male ratio was 1:1 and a similar ratio was reported in other studies[19,20] while, another study reported higher incidence in females (2:1)[21]. All newborns who are initially positive on spot test but are negative on ELISA could be due to iodine deficiency in mothers[22]. A significant association between parental consanguinity and congenital hypothyroidism has been reported in neonates with 1st cousin parental consanguinity than 2nd cousin parental consanguinity[23]. In Pakistan 1st and 2nd parental consanguinity is common but no such association was seen in the present study.

Newborn screening was able to diagnose twice many cases of CH as compared to countries where no screening was done[2]. In Pakistan there is a need to establish a newborn screening facility at national level, in all public and private sector hospitals which have a maternity unit attached to them so as to facilitate early diagnosis and treatment of hypothyroid cases.

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