Original Article

Congenital hypothyroidism in neonates

Aneela Anjum, Muhammad Faheem Afzal, Syed Muhammad Javed Iqbal, Muhammad Ashraf Sultan, Asif Hanif[1]

Department of Paediatrics, King Edward Medical University/Mayo Hospital, [1]Biostatistics, PGMI, Gulab Devi Hospital, Lahore, Pakistan

ABSTRACT

Context: Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation in children and it occurs in approximately 1:2,000-1:4,000 newborns. **Aims and Objectives:** The aim of this study is to determine the frequency of CH in neonates. **Settings and Design:** This cross-sectional study was conducted in neonatal units of the Department of Pediatrics Unit-I, King Edward Medical University/Mayo Hospital, Lahore and Lady Willington Hospital Lahore in 6 months (January-June 2011). **Materials and Methods:** Sample was collected by non-probability purposive sampling. After consent, 550 newborn were registered for the study. Demographic data and relevant history was recorded. After aseptic measures, 2-3 ml venous blood analyzed for thyroid-stimulating hormone (TSH) level by immunoradiometric assay. Treatment was started according to the individual merit as per protocol. **Statistical Analysis Used:** Data was analyzed by SPSS 17 and Chi-square test was applied to find out the association of CH with different variables. **Results:** The study population consisted of 550 newborns. Among 550 newborns, 4 (0.8%) newborns had elevated TSH level. CH had statistically significant association with mother's hypothyroidism (*P* value 0.000) and mother's drug intake during the pregnancy period (*P* value 0.013). **Conclusion:** CH is 0.8% in neonates. It has statistically significant association with mother's hypothyroidism and mother's drug intake during pregnancy.

Key words: Congenital hypothyroidism, newborn, thyroid-stimulating hormone

Introduction

Congenital hypothyroidism (CH) is defined as thyroid hormone deficiency present at birth.[1] Thyroid hormone plays a vital role in normal development of the central nervous system. Deficiency of thyroid hormone is one of the most common preventable causes of mental retardation.[2] CH occurs in approximately 1:2,000-1:4,000 newborns. The clinical manifestations are often subtle or not present at birth. Common symptoms include decreased activity and increased sleep, feeding difficulty, constipation and prolonged jaundice while myxedematous facies, large fontanels, macroglossia, a distended abdomen with umbilical hernia and hypotonia are common signs.[1]

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.129114

Hypothyroidism in the newborn period is almost always overlooked and delayed diagnosis leads to the most severe outcome, mental retardation, emphasizing the importance of neonatal screening. Neonatal screening for CH must be carried out by the 5th day of the child's life at the latest.[3] Blood spot T4 or thyroid-stimulating hormone (TSH) or both can be used in neonatal screening for CH. The diagnosis should be confirmed by finding an elevated serum TSH.[4] Initial preliminary studies were performed using TSH levels in cord blood.[5,6] Mass screening was made feasible by the development of radioimmunoassay for TSH and thyroxine (T4) from blood spots on filter paper, obtained for neonatal screening tests. Studies in Pakistan to find the incidence have been few and on a smaller scale, but predict a much higher incidence of 1:1000.[7] One study carried out in Lahore in 2003 shows that approximately 2% newborns are suffering from CH.[8]

Local data to demonstrate the burden of CH is lacking. Therefore, this study was planned to find out frequency of CH so that early detection and treatment may be performed to prevent the mental retardation and other complications.

Corresponding Author: Dr. Muhammad Faheem Afzal, Department of Paediatrics, Unit-I, King Edward Medical University/Mayo Hospital, Lahore, Pakistan. E-mail: mfaheem169@yahoo.com

Materials and Methods

This cross-sectional observational study was conducted in the Neonatal units of the Department of Pediatrics Unit-I, King Edward Medical University/Mayo Hospital, Lahore and Lady Willington Hospital Lahore from January to June 2011. Mayo Hospital, Lahore is a government funded tertiary care hospital affiliated with King Edward Medical University (previous King Edward Medical College). Department of Pediatric Medicine of this hospital is having its own emergency, intensive care unit and neonatology. Neonatal unit of Lady Willington Hospital Lahore is affiliated with Pediatric Medicine Unit-I, King Edward Medical University/Mayo Hospital Lahore. Sample was collected by non-probability purposive sampling. After consent from parents, 550 healthy newborns of both the genders with birth weight >2.5 kg from 4th to 7th day of life were registered for the study. Sample size of 550 cases was calculated with 90% confidence level, 1% margin of error and taking expected percentage of CH, i.e., 2% in neonates attending the well-baby clinic of a tertiary care hospital. Critically sick newborns (those requiring neonatal admissions and critical care) and premature (<37 weeks of gestation as mentioned in the record) were excluded. Demographic data including name, age, sex, weight, gestational age, maternal age and address was recorded. History of any thyroid disease in mother and use of anti-thyroid drugs by mother in pregnancy was also recorded for accurate interpretation of laboratory data. After aseptic measures, 2-3 ml venous blood was taken and sent to Center for Nuclear Medicine of Mayo Hospital, Lahore for TSH level, where it was analyzed by immunoradiometric assay. Those neonates having serum level of TSH >20 mIU/L were labeled as cases of CH. Since, the study was self-funded; we could not perform T4 level due to the financial reasons. Treatment was started according to the individual merit as per protocol. All the information was recorded on specially designed proforma. Data of all the cases was entered into SPSS version 17 program and analyzed for statistical package. Socio-demographic data such as mother's age, weight, gestational age, was presented as mean and standard deviation. The qualitative data such as sex, history of any thyroid disease in mother, use of anti-thyroid drugs by mother during pregnancy and TSH results were presented as frequency tables. Chi-square test was applied to find out association of CH with mother's age, newborn's sex, weight and gestational age, history of any thyroid disease in mother and use of anti-thyroid drugs by mother during pregnancy.

Results

The study population consisted of 550 newborns. Mothers' age range was 18-45 years with a mean age of 26 ± 4 years. A total of 249 (45%) mothers were 26-30 years of age. Among the total population of 550 newborns, 287 (52%) were male, 546 (99.2%) were born at gestational age of ≥37-40 weeks while 342 (62%) had a birth weight of >2.5-3 kg. Out of total, only 3 (0.6%) mothers of these newborn had a history of hypothyroidism while only 1 (0.2%) mother of these newborn had a history of drug intake for hypothyroidism during pregnancy [Table 1]. Among 550 newborns, 546 (99.2%) had normal level of TSH while 04 (0.8%) newborns had elevated TSH level. Hence frequency of CH was 0.8% [Figure 1]. Mean TSH level was 6.2 ± 4 mIU/l. When data was analyzed for association of CH with above variables, it was found that CH had statistically significant association with mother's hypothyroidism (*P* value 0.000) and mother's drug intake during pregnancy (*P* value 0.013) [Table 2].

Discussion

The present study population consisted of 550 newborns. Mothers' age range was 18-40 years with a mean age of 26 ± 4 years. These results are in accordance with the study by Adeniran *et al*.[9] in which most of the mothers were above 25 years of age. Similar results were also reported previously in Pakistan by Karam *et al*.[10]

In our study, male to female ratio of newborn was 1.1:1. These results are in supported by international[11] and local data.[8,10] However, Adeniran *et al*.[9] reported female

Table 1: Demography (*n*=550)

Variable	*n* (%)
Mother's age (years)	
≥18-25	175 (32)
26-30	249 (45)
>30	126 (23)
Mean±SD	26±4 years
Sex	
Male	287 (52)
Female	26 (48)
Gestational age (weeks)	
≥37-40	546 (99.2)
>40	04 (0.8)
Mean±SD	38±1 week
Birth weight (kg)	
>2.5-3	342 (62)
3.1-3.5	191 (35)
>3.5	17 (03)
Mean±SD	2.9±0.3 kg
Mode of delivery	
Cesarean	358 (65)
Vaginal	192 (35)
Maternal history of hypothyroidism	
Yes	03 (0.6)
No	547 (99.4)
Anti-thyroid drug intake during pregnancy	
Yes	01 (0.2)
No	549 (99.8)

SD: Standard deviation

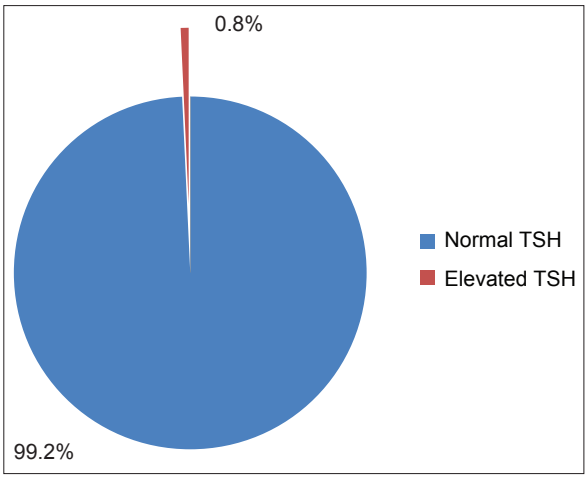

Figure 1: Distribution of cases by thyroid-stimulating hormone level (*n*=550)

preponderance. In the present study, 546 (99%) were born at gestational age of ≥37-40 weeks while 4 (1%) were born at gestational age of >40 weeks. Mean gestational age was 38 ± 1 week. These results are in accordance with the study by Adeniran *et al*.[9] where authors found the majority of newborns between 37 weeks and 39 weeks of gestation. The reason of having newborns ≥37 weeks is due to the fact that we did not include preterm babies in our study. Present study had 342 (62%) newborn with birth weight of >2.5-3 kg, 191 (35%) had a birth weight of 3.1-3.5 kg while 17 (03) were above 3.5 kg. Mean birth weight was 2.9 ± 0.3 kg. These results are in accordance with the study by Adeniran *et al*.[9] in which authors found the majority of newborns appropriate for the age. Similarly, our results are also supported in Pakistan by Abbas *et al*.[8] However, Ward *et al*.[11] found low birth weight newborns in their study. The difference may be due to the fact that we did not include low birth weight newborns in the present study.

During gestation, maternal and fetal thyroid functions are autonomously regulated yet they are not independent of one another. Fetal thyroid activity depends entirely on the availability of iodine transferred from maternal circulation.[10] In our study, only 3 (0.6%) mothers of the newborn had a history of hypothyroidism while 1 (0.2%) mother used drugs for hypothyroidism during pregnancy. International[12] and local[8,10] studies have comparable results where authors found that mothers suffering from hypothyroidism are likely to give birth to newborn having CH.

Elevated serum TSH level in neonates indicates insufficient supply of thyroid hormone to the developing brain. International organizations such as World Health Organization and United Nations Children's Fund have included neonatal TSH as one of the indicators for assessing iodine deficiency disorders.[10,12] Detection of CH by newborn screening program relies on the

Table 2: Association of congenital hypothyroidism (*n*=550)

Variable	Hypothyroidism based on TSH level		Total	*P* value
	Normal	Congenital hypothyroid		
Mother's age (years)				
≥18-25	175	2	177	0.801
26-30	248	1	249	
>30	123	1	124	
Sex				
Male	284	3	287	0.552
Female	262	1	263	
Gestational age (weeks)				
≥37-40	542	4	546	0.801
>40	4	0	4	
Birth weight (kg) t				
>2.5-3	339	3	342	0.833
3.1-3.5	190	1	191	
>3.5	17	0	17	
Maternal history of hypothyroidism				
Yes	0	3	3	0.000
No	546	1	547	
Maternal history of anti-thyroid drug intake				
Yes	0	1	1	0.013
No	546	3	549	

TSH: Thyroid-stimulating hormone

immunoassay measurement of various combinations of thyroid hormones. Total T4 is not the same as free T4. Free T4 is a more accurate read of thyroid hormone. Free T4 measures the free, unbound thyroxine T4 levels in the bloodstream and is typically generally lowered in hypothyroidism. However, many newborn screening program programs, including those in Australasia, perform a single TSH test due to its simplicity and relatively low false positive rate compared with combined strategies. This strategy will not detect central hypothyroidism and low birth weight and premature babies are a potential source of false negative screens due to hypothalamic immaturity and thus require a second sample. We did not include critically sick or premature babies.[13] However, due to financial reasons, we could not perform T4 level along with TSH for neonatal screening.

The present study had 546 (99.2%) had normal level of TSH while 04 (0.8%) newborns had elevated TSH level. Hence, frequency of CH was 0.8%. Our results are supported by international and national data. Manglik *et al*.[14] in India found 22 babies out of 1200 had TSH >20 mIU/L within first 24 h, while the test was when repeated on 7th day, CH was confirmed in 2 babies. Hence CH in his study was 0.16%. van Tijn *et al*.[15] conducted his study on a larger scale (385,000 newborn over 2 years period) and found 19 cases of CH with permanent brain damage. This emphasizes the importance of neonatal screening program

and implementation of timely treatment. Abbas *et al*.[8] in Pakistan studied serum TSH level as a screening tool for CH in a tertiary care hospital and found mean TSH level 5.6 ± 5.1 mIU/L. Authors found CH in 2% of cases. The results of the study are comparable with those of the present study.

In the present study, we found that CH had statistically significant association with mother's hypothyroidism and mother's drug intake during pregnancy. Local and international data supports our results. Manglik *et al*.[14] found statistically significant association of CH with mother's hypothyroidism. Authors also found that CH was more common in newborn, whose hypothyroid mothers did not take the anti-thyroid drug during pregnancy. Similar observations were made by Ward *et al*.[11] in USA and Abbas *et al*.[8] and Karam *et al*.[10] in Pakistan.

Present study has certain limitations. We could not perform T4 level along with TSH for neonatal screening. This would not detect central hypothyroidism. This would not precisely able to differentiate between true or physiological rise in TSH. However, since Neonatal screening for CH is recommended by the 5th day of the child's life at the latest. Therefore, we believe that we have performed the screening between 4th day and 7th day of life; the rise in TSH in the present study might be true. It was carried out with the exclusion of low birth weight and preterm babies. If the study had been performed including these babies on a larger scale, the results might have been different. Lastly, follow-up of study at 3 months of age was not performed to rule out transient hypothyroidism.

Conclusion

Frequency of CH is 0.8% in neonates attending a tertiary care hospital. CH has statistically significant association with mother's hypothyroidism and mother's drug intake during pregnancy.

References

1. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis 2010;5:17.
2. Bernal J. Action of thyroid hormone in brain. J Endocrinol Invest 2002;25:268-88.
3. Pitt JJ. Newborn screening. Clin Biochem Rev 2010;31:57-68.
4. Büyükgebiz A. Newborn screening for congenital hypothyroidism. J Pediatr Endocrinol Metab 2006;19:1291-8.
5. Klein AH, Agustin AV, Foley TP Jr. Successful laboratory screening for congenital hypothyroidism. Lancet 1974;2:77-9.
6. Buist NR, Murphey WF, Brandon GR, Foley TP Jr, Penn RL. Letter: Neonatal screening for hypothyroidism. Lancet 1975;2:872-3.
7. Malik BA, Butt MA. Is delayed diagnosis of hypothyroidism still a problem in Faisalabad, Pakistan. J Pak Med Assoc 2008;58:545-9.
8. Abbas HG, Elahi S, Khan MS, Naeem M. Serum thyroxine and thyroid stimulating hormone levels in cord blood of newborns in Lahore. Pak J Med Sci 2003;19:211-6.
9. Adeniran KA, Okolo AA, Onyiriuka AN. Thyroid profile of term appropriate for gestational age neonates in Nigeria: A forerunner to screening for congenital hypothyroidism. J Trop Pediatr 2010;56:329-32.
10. Karam GA, Hakimi H, Rezaeian M, Gafarzadeh H, Rashidinejad H, Khaksari M. Thyroid function in mothers who gave birth to neonates with transient congenital hypothyroidism. Pak J Med Sci 2009;25:568-2.
11. Ward LS, Kunii IS, de Barros Maciel RM. Thyroid stimulating hormone levels in cord blood are not influenced by non-thyroidal mothers' diseases. Sao Paulo Med J 2000;118:144-7.
12. American Academy of Pediatrics, Rose SR, Section on Endocrinology and Committee on Genetics, American Thyroid Association, Brown RS, Public Health Committee, Lawson Wilkins Pediatric Endocrine Society, Foley T, *et al*. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics 2006;117:2290-303.
13. Pezzuti IL, Lima PP, Dias VM. Congenital hypothyroidism: The clinical profile of affected newborns identified by the Newborn Screening Program of the State of Minas Gerais, Brazil. J Pediatr (Rio J) 2009;85:72-9.
14. Manglik AK, Chatterjee N, Ghosh G. Umbilical cord blood TSH levels in term neonates: A screening tool for congenital hypothyroidism. Indian Pediatr 2005;42:1029-32.
15. van Tijn DA, de Vijlder JJ, Verbeeten B Jr, Verkerk PH, Vulsma T. Neonatal detection of congenital hypothyroidism of central origin. J Clin Endocrinol Metab 2005;90:3350-9.

Cite this article as: Anjum A, Afzal MF, Iqbal SJ, Sultan MA, Hanif A. Congenital hypothyroidism in neonates. Indian J Endocr Metab 2014;18:213-6.

Source of Support: Nil, **Conflict of Interest:** None declared.