

ORIGINAL ARTICLE

FREQUENCY OF NEONATAL THYROID DISORDERS IN A TERTIARY CARE HOSPITAL IN KARACHI

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ABSTRACT

Background: Thyroid hormone is necessary for metabolism, growth and brain development. Thyroid-stimulating hormone (TSH) secreted by anterior pituitary gland acts on thyroid to release thyroid hormones T3 and T4. Insufficient production of thyroid hormone at birth is known as congenital hypothyroidism (CH). CH leads to intellectual impairment, if not identified. Neonatal hyperthyroidism is relatively uncommon. The objective of this study is to determine the frequency of thyroid disorders in neonates born in a tertiary care hospital.

Methods: This is retrospective cross-sectional, observational study carried out at the tertiary care hospital Karachi, from October 2017 to May 2018. Screening for thyroid disorders is mandatory for newborns born in our hospital. Only data of neonates with thyroid stimulating hormone (TSH) performed was included for this study. TSH levels of these patients were determined by immunoassay on Vitros Enhanced Chemiluminescence technique.

Results: In this study, 383 neonates were included, who were born in Ziauddin Hospital Clifton and /or were presented in Ziauddin hospital laboratory for TSH testing. The average age of neonates was 4.11+/-4.14 days and average TSH levels were 4.58+/-4.32 µIU/ ml. They were divided into two groups: Group# I from birth to 4days of life, 305 neonates were included in which 278(91.1%) were euthyroid and 27(8.9%) were hyperthyroid. None of neonates found hypothyroid in this age group. Group# II from 5 days to 1 month of life, only 78 neonates were included, 55(70.5%) were euthyroid, 18(23.1%) were hypothyroid and 5(6.4%) were hyperthyroid.

Conclusion: Neonatal screening for thyroid disorders is very beneficial for patients as well as their families and also gives information regarding these disorder's epidemiology, pathophysiology, diagnosis and treatment in infantile period.

KEYWORDS: Thyroid Stimulating Hormone (TSH), Congenital Hypothyroidism (CH), Hyperthyroid.

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INTRODUCTION

Thyroid hormone is a small butterfly shaped gland partially encircling the trachea. It is necessary for metabolism, growth and brain development¹. The thyrotropin-releasing hormone released by hypothalamus acts on anterior pituitary gland to secrete thyroid-stimulating hormone (TSH). TSH in turn acts on thyroid gland to release thyroid hormones, T3 and T4². The thyroid levels in blood are controlled by

negative feedback mechanism. Thyroid hormones are required for promoting protein synthesis, growth regulation, and affects carbohydrate, lipid, and vitamin metabolism³.

Insufficient production of thyroid hormone at birth is known as congenital hypothyroidism (CH)¹. It is the most preventable cause of intellectual impairment. It leads to growth failure, irreversible mental retardation, a variety of neuropsychological deficits and

cretinism^{4,5}. CH has two types, transient and permanent. In transient hypothyroidism, infants are temporarily deficient, whereas the permanent type requires lifetime hormone therapy⁶. Clinical diagnosis is not possible due to nonspecific signs and symptoms e.g. prolonged jaundice, umbilical hernia, feeding difficulty, lethargy, etc⁷. Treatment is cheap and effective. Hence, with early detection and treatment, infants usually develop normally without physical or mental handicaps⁸.

Neonatal hyperthyroidism is uncommon and not frequently observed as CH. It is related to maternal Graves' disease⁹.

Factors that affect neonatal TSH concentration are mode of delivery, pregnancy duration, and maternal thyroid status^{10,11}.

The American Academy of Pediatrics recommends thyroid screening in neonates¹². There are three types of screening method; primary TSH with backup T4 measurements, primary T4 with backup TSH measurements, and combined primary TSH and T4 measurements. Primary TSH approach mostly followed. It is usually performed within 2–4 days of life to avoid false positive tests resulting from initial TSH surge^{13,14}. This also rules out transient hypothyroidism. Routinely serum from whole blood or heel prick is used, but TSH levels can be assessed in cord blood as well¹³. In Europe and North America, it is done on Guthrie paper with a drop of neonate's blood hereafter analysis by immunoassay, which is simple and inexpensive¹⁴. Sadly, this is not yet introduced in Pakistan.

The worldwide annual incidence of CH is 1: 4000 live birth¹⁵. However, in developing countries like India, Bangladesh and Pakistan it is higher because of lack of established screening program^{16, 17, 18}. In Pakistan, only a few hospitals in the private sector carry it as a routine neonatal care measure. Therefore, the magnitude of this problem largely remains unknown. The purpose of this study is to determine the frequency of thyroid disorders in neonates born in a tertiary care hospital.

METHODS

This is retrospective cross-sectional, observational

study carried out at the tertiary care hospital Karachi, from October 2017 to May 2018. Screening for thyroid disorders is mandatory for newborns born in the hospital. Only data of neonates with thyroid stimulating hormone (TSH) performed was included for this study. TSH levels of these patients were determined by immunoassay on Vitros Enhanced Chemiluminescence technique.

TSH levels of the neonates were retrieved from hospital records. Neonates were interpreted as hypothyroid, euthyroid and hyperthyroid using age reference ranges of TSH that were available in our lab, i.e. birth to 4 days of life – 1.0-7.39.0 µIU/ml and 5 days to 1 month – 0.7-4.8 µIU/ml. We excluded premature babies that were born 28 to 36 weeks of gestational life and cord blood samples of > 37 weeks.

TSH values below reference were labeled as hyperthyroid while above reference were labeled as hypothyroid. Within reference range, neonates were called euthyroid.

Statistical Analysis was done on SPSS version 20.

RESULTS

In this study, 383 neonates were included, who were born in Ziauddin Hospital (Clifton) and /or were presented in Ziauddin Hospital laboratory for TSH testing.

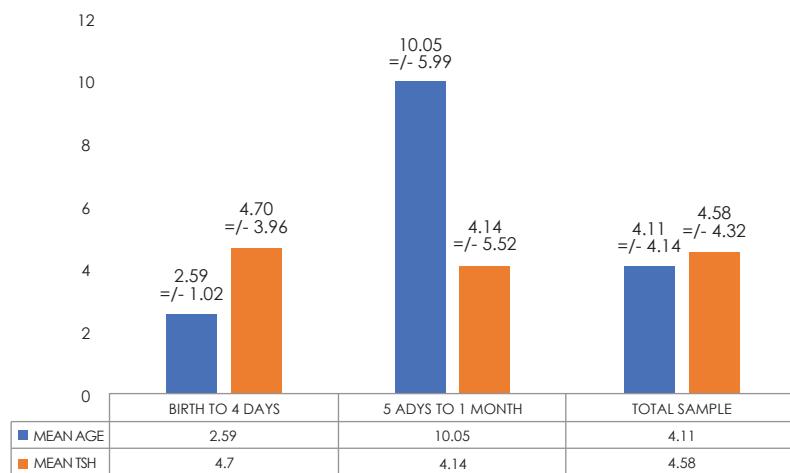
We divided them into two groups: Group 1 from birth to 4days of life, total 305 neonates were included in which 278(91.1%) were euthyroid and 27(8.9%) were hyperthyroid. None of neonates found hypothyroid in this age group (Table 1).

In Group 2 from 5 days to 1 month of life, only 78 neonates were included in which 55(70.5%) were euthyroid, 18(23.1%) were hypothyroid and 5(6.4%) were hyperthyroid (Table 1).

The average age of all neonates was 4.11+/-4.14 days and average TSH levels were 4.58+/-4.32 µIU/ml (figure 1). Male to female ratio was not calculated because neonates were registered with name of his/her mother's name.

TABLE 1: THE FREQUENCY OF THYROID STATUS IN TWO GROUPS OF NEONATES.

GROUPS	THYROID STATUS	FREQUENCY N (%)
GROUP 1: BIRTH TO 4 DAYS	HYPERTHYROID	27(8.9)
	EUTHYROID	278(91.9)
GROUP 2: 5 DAYS TO ONE MONTH	HYPERTHYROID	5 (6.4)
	HYPOTHYROID	18 (23.1)
	EUTHYROID	55 (70.5)

**Figure 1: Comparison of age with TSH levels in neonates.**

DISCUSSION

Maternal thyroid hormone crosses placenta to the fetus and aids brain development¹⁹. However, from 20th week of gestation, the neonatal thyroid tissue begins synthesizing TSH and T4 hormones independently^{20, 21}. Immediately following the birth there occurs a sudden sharp surge of TSH levels (closely followed by T4 levels) reaching a peak in the first 30 minutes, thereafter followed by a gradual decline over the next 3-4 days, therefore variation in thyroid function tests is seen during the first week of life. Most screening programs suggest drawing samples after the 4th day of life²¹. Majority of the tertiary care hospitals including ours, babies are discharged by the 3rd to 4th day; therefore, blood is usually drawn between 48-72 hours. TSH values are interpreted with the age of the neonate.

In the absence of national thyroid screening program, any related data is valuable. In this study 305 neonates born between birth to 4th day were

screened and only 27(8.9%) had TSH levels less than 1 µIU/ml, hence found hyperthyroid. This is most likely due to heightened metabolism²². Congenital hyperthyroidism is rare and mostly due maternal thyrotoxicosis or a genetic mutation of the thyroid-stimulating hormone receptor (TSHR)²². Therefore, TSH should be repeated after few days along with detail maternal history.

Out of 78 neonates age range between 5th day to 1 month of life screened, 18(23.1%) were hypothyroid. Hypothyroidism if transient is due to maternal antithyroid medications, maternal antibodies, excessive neonatal iodine expose and prolonged hospitalization due to illness^{14, 22, 23}. Permanent hypothyroidism is synonymous to CH. In 80-85% cases, the thyroid gland is absent, small or located abnormally, while in the rest, normal to large sized thyroid gland is present but production is decreased or absent¹. Ever since screening is done routinely in many countries, twice the number of CH are identified compared to those countries where it

is not done⁴.

Due to small sample size, our study showed a high number of neonates with hypothyroidism. In other local studies, Noreen et al., showed 16.3% of the neonates had hypothyroidism, Ghaffor et al. reported CH incidence 2 out of 1357 cases^{2,1}. A study by Afroze et al., only 10 babies were diagnosed with congenital hypothyroidism initially but after follow up final incidence rate was 1 in 1600 live births²⁴. Ahmad et al. showed out of 3 out of 767 neonates were hypothyroid. They also found an association between mode of delivery and CH. It was higher in neonates born through C-section²⁵. Seth et al. observed higher TSH levels in neonates born through forceps extraction²⁶. This proves that mode of delivery affects neonatal TSH levels. Since our hospital is a tertiary care private hospital, chances of C-sections /forceps delivery might be higher so can be reason behind higher cases of neonatal hypothyroidism.

CH is more frequently seen in females than males, the ratio is 2:1. This has been reported locally as well as internationally^{15, 25, 27}. In our study, the gender could not be retrieved, as it was a retrospective data.

5 out 74 neonates (6.4%) were found to be hyperthyroid screened between 5th day to 1 month of life, most likely due to maternal reasons⁹.

Due to small sample size, no definite conclusion could be drawn. However, our study has shown the importance of neonatal thyroid screening. About 10–15% pregnant women suffer from thyroid dysfunction during pregnancy and subclinical hypothyroidism is 4–8.5% prevalent globally¹⁹. Hence, maternal factors should be considered when TSH levels are interpreted. Parental awareness regarding the importance of thyroid screening is also essential. There is dire need to establish newborn screening as well as follow-up facility at national levels in public as well as private hospitals.

CONCLUSION

Neonatal screening for thyroid disorders is very beneficial for patients as well as their families and also gives information regarding these disorder's epidemiology, pathophysiology and diagnosis in infantile period.

REFERENCES

- Ghafoor F, Mohsin SN, Mukhtar S, Younas S, Hussain W. Newborn screening for congenital hypothyroidism in a public sector hospital. Pak J Med Res 2013;52(2):39.
- Noreen R, Memon MH, Murtaza G, Hanif S. Frequency of Congenital Hypothyroidism (CH) in Neonates of a Tertiary Care Hospital of Karachi, Pakistan. Ann Abbasi Shaheed Hosp Karachi Med Dent Coll 2016;21(2):75-81.
- Kliegman RM, Behrman RE, Jenson HB, Stanton BM, editors. Nelson Textbook of Pediatrics. 19th Ed. Philadelphia: Saunders; 2008.
- Newborn screening fact sheets. American Academy of Pediatrics. Pediatrics 1989;83(3):449-64.
- Willi SM, Moshang Jr T. Diagnostic dilemmas: results of screening tests for congenital hypothyroidism. Pediatr Clin North Am 1991;38(3):555-66.
- Bona G, Bellone S, Prodam F, Monzani A. Etiology of Congenital Hypothyroidism In Thyroid Diseases in Childhood 2015 (pp. 27-31). Springer, Cham.
- Karamizadeh Z, Saneifard H, Amirhakimi G, Karamifar H, Alavi M. Evaluation of congenital hypothyroidism in Fars province, Iran. Iran J Pediatr 2012;22(1):107.
- Tariq B, Ahmed A, Habib A, Turab A, Ali N, Soofi SB, Nooruddin S, et al. Assessment of knowledge, attitudes and practices towards newborn screening for congenital hypothyroidism before and after a health education intervention in pregnant women in a hospital setting in Pakistan. Int Health 2018;10(2):100-7.
- Lourenço R, Dias P, Gouveia R, Sousa AB, Oliveira G. Neonatal McCune-Albright syndrome with systemic involvement: a case report. J Med Case Rep 2015;9(1):189.
- Herbstman J, Apelberg BJ, Witter FR, Panny S, Goldman LR. Maternal, infant, and delivery factors associated with neonatal thyroid hormone status. Thyroid 2008;18(1):67-76.
- Trumpf C, Vandevijvere S, Moreno-Reyes R, Vanderpas J, Tafforeau J, Van Oyen H, De Schepper J. Neonatal thyroid-stimulating hormone level is influenced by neonatal, maternal, and pregnancy factors. Nutr Res 2015;35(11):975-81.
- Lone SW, Ibrahim MN, ATTA I LT, Khan YN, Raza J. Nine years experience of congenital hypothyroidism, an urgent need for mandatory newborn screening. Pak Paedr J 2010;34(3):123-7.
- Chaudhary M, Soni JP, Goyal VK, Sharma P, Makwana M, Lora SS. Incidence of congenital hypothyroidism in Western Rajasthan using cord blood thyroid-stimulating hormone levels as a screening tool: A cross-sectional hospital-based study. Indian J Endocrinol Metab 2018; 22(3):417.
- 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, Kaplowitz PB, Kaye CI, Sundararajan S, Varma SK. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics 2006;117(6):2290-303.
- Deladoëy J, Van Vliet G. The changing epidemiology of congenital hypothyroidism: fact or artefact? Expert Rev Endocrinol Metab 2014;9(4):387-95.
- Lorey FW, Cunningham GC. Birth prevalence of primary congenital hypothyroidism by sex and

- ethnicity. *Human Biol* 1992;64(4):531-8.
17. Pande S. Neonatal hypothyroidism. International Advisory cum Editorial Board: 16.
 18. Lakhani M, Khurshid M, Naqvi SH, Akber M. Neonatal screening for congenital hypothyroidism in Pakistan. *J Pak Med Assoc* 1989;39:282.
 19. Fatima SS, Rehman R, Butt Z, Asif Tauni M, Fatima Munim T, Chaudhry B, Khan TA. Screening of subclinical hypothyroidism during gestational diabetes in Pakistani population. *J Matern Fetal Neonatal Med* 2016;29(13):2166-70.
 20. Schmaltz C. Thyroid hormones in the neonate: an overview of physiology and clinical correlation. *Adv Neonatal Care* 2012;12(4):217-22.
 21. Allen DB, Sieger JE, Litsheim T, Duck SC. Age-adjusted thyrotropin criteria for neonatal screening for hypothyroidism. *J Pediatr* 1990;117(2):309-12.
 22. Delahunty C, Falconer S, Hume R, Jackson L, Midgley P, Mirfield M, et al. Scottish Preterm Thyroid Group. Levels of neonatal thyroid hormone in preterm infants and neurodevelopmental outcome at 5 1/2 years: millennium cohort study. *J Clin Endocrinol Metab* 2010;95(11):4898-908.
 23. Afroze B, Humayun KN, Qadir M. Newborn screening in Pakistan—lessons from a hospital-based congenital hypothyroidism screening programme. *Ann Acad Med Singapore* 2008;37(12 Suppl):114-3.
 24. Adeel Ahmad AW, Hussain S, Saeed M, Ahmad BM, ur Rehman K. Congenital Hypothyroidism in Neonates of a Tertiary Care Hospital. *Pak J Med Sci* 2017;33(5):1269.
 25. Seth A, Sekhri T, Agarwal A. Effect of perinatal factors on cord blood thyroid stimulating hormone levels. *J Pediatr Endocrinol Metab* 2007;20(1):59-64.
 26. Unachak K, Dejkhamron P. Primary congenital hypothyroidism: clinical characteristics and etiological study. *J Med Assoc Thai* 2004;87(6):612-7.
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