DOI: https://doi.org/10.53350/pjmhs020231712281

ORIGINAL ARTICLE

Incidences of Congenital Hyperthyroidism in Neonates Born to Hyperthyroid Women

ZAHIDA KAMAL[1], HABIBULLAH BABAR[2], SHAMAYAL MANDOKHEL[3]
[1]Consultant Gynaecologist, Gynae Unit 2, Bolan Medical Complex Hospital, Quetta
[2]Professor, [3]Associate Professor, Department of Paediatrics, Balochistan Institute of Child Health Services Quetta
Correspondence to: Zahida Kamal, E-mail: zahidayousaf2011@gmail.com, Cell: 0333-7786144

ABSTRACT

Background: Thyroid hormones are important not only for the development of the central nervous system of infants but also play a vital role in regulation of various metabolic activities during infancy. Recent advances in literature have identified the risk of congenital hypo-hyperthyroidism in infants whose mother is suffering from hyperthyroidism.

Objective: To estimate the incidence of congenital hyperthyroidism in neonate born to hyperthyroid women.

Study Design: Prospective cohort study

Place and Duration of Study: Department of Gynaecology, Bolan Medical Complex Hospital Quetta from 1st January 2021 to 30th September 2023.

Materials and Methods: Five hundred pregnant women who were suffering from hyperthyroidism were enrolled. The complete demographic details, prima, gravida, body mass index, hypertension, comorbidities were entered in a well-structured questionnaire. Each pregnant woman underwent 3cc blood withdrawal for analyzing her thyroid function test and confirmation the hyperthyroidism. Each pregnant woman was followed up to their delivery. Each baby was sent to Baluchistan Institute of Health Science, Quetta for Thyroid stimulating test which was performed through a blood spot pricked from the newborns heal using pricking lancet. The test was performed within 24-72 hours post-delivery. The maternal antibodies were also analyzed from the same blood spot through enzyme linked immune sorbent assay. Those cases which were identified with congenital hyperthyroidism were further treated for complete assessment and treatment at Balochistan Institute of Child Health Service Quetta. Those neonates with high, subclinical or borderline conditions were referred to a repeat test after 3-5 days, 15 days and 30 days after birth for reassessment and follow up.

Results: Majority of the pregnant hyperthyroid women were within the age group of 26-40 years with an overall mean age of 27.8±2.85 years. There were 87.6% those women who showed the presence of autoantibodies in them. Out of the total number of singleton deliveries there were 79.6% of the neonates born with normal body weight while 20.4% were found to be underweight. There were three neonates born with hyperthyroidism detected within the first 72 hours of their life.

Conclusion: The overall incidence of congenital hyperthyroidism neonates within pregnant women suffering from hyperthyroidism was reported as 0.6%.

Keywords: Incidence, Congenital hyperthyroidism, Neonates**,** Hyperthyroid women

INTRODUCTION

Thyroid gland is an endocrine gland situated constituted of two connected lobes situated in the neck of vertebrates. The hormones released by the thyroid gland are associated with metabolic control and other functions of the body system.[1-3] The role of various hormones during infancy is highly significant for the proper growth and development of the neonate. Thyroid hormones are important not only for the development of the central nervous system of infants but also play a vital role in regulation of various metabolic activities during infancy.[4]

Routine screening of thyroid hormones for neonates was initiated early in 1990s. Until now there is a deficiency of consensus data which can verify on identifying precise risk factors leading to congenital hyperthyroidism.[5-7] Graves' disease is an autoimmune disorder that causes hyperthyroidism (an overactive thyroid gland). A combination of genetic and environmental factors including family history, gender, age, stress, loss of vitamins and mineral as well as medical conditions can lead to Graves' disease.[8,9]

Recent advances in literature have identified the risk of congenital hypo-hyperthyroidism in infants whose mother are suffering from Graves disease depending upon the balanced reached between thyrotropin (TSH) receptor stimulating as well as binding antibiotics and antithyroid drugs during their placental passage.[3] The incidence of neonatal hyperthyroidism may be presented in 1 to 5% of the offspring's born to the mothers suffering with Grave's disease. The incidence has been reported without gender discrimination. Since the global prevalence of Grave's disease itself is only 0.2% leading to 1 out of the total 25-50 thousand births having the risk of congenital hyperthyroidism. The prevalence of hyperthyroidism in Pakistan is 2.9%, which is two times higher than in the United States.[5,8]

The neonatal hyperthyroidism is self-limited and resolves within the first six months of life (within week 3 to 13), yet it can become life threatening and requires early diagnosis and treatment for avoiding criticalities.[10,11] The present study was designed to assess the incidence of congenital hyperthyroidism in neonates born to hyperthyroid women. The results of this study provided substantial evidence on the extent of maternal hyperthyroidism as a risk factor for development of hyperthyroidism in neonates.

Received on 01-10-2023
Accepted on 28-11-2023

MATERIALS AND METHODS

This prospective cohort study was conducted at Department of Gynaecology, Bolan Medical Complex Hospital Quetta from 1st January 2021 to 30th September 2023. All those pregnant women who were suffering from hyperthyroidism were enrolled as study participants after their consideration of the written informed consent. The total number of patients received within the two years was 500. The sample size was estimated using the already known prevalence of hyperthyroidism in Pakistan while the sample size calculation was performed through available software which applies 95% CI, and 80% power of test. The complete demographic details, prima, gravida, body mass index, hypertension, comorbidities were entered in a well-structured questionnaire. Each pregnant woman underwent 3cc blood withdrawal for analyzing her thyroid function test and confirmation of hyperthyroidism. Pregnant women who were confirmed for hyperthyroidism, singleton pregnancy, between the age group 18-40 years were included in this study. Those pregnant women having subclinical hyperthyroidism, serious comorbidities, autoimmune disorders were excluded from the study. Each pregnant woman was followed up to their delivery. The Thyroid stimulating test of each baby was sent to Baluchistan Institute of Health Science, Quetta which was performed through a blood spot pricked from the newborns heal using pricking lancet. The test was

performed within 24-72 hours post-delivery. The maternal antibodies were also analyzed from the same blood spot through enzyme linked immune sorbent assay. The maternal antibodies were also analyzed from the same blood spot through enzyme linked immune sorbent assay. The analysis was done through formation of filter blot and assessing the blood spot on filter paper by gamma counter application. Newborns vitals, weight and health status was assessed at Baluchistan Institute of Child health Services Quetta by a pediatrician. Newborns weight, mode of delivery, gestational age was documented. Those cases which were identified with congenital hyperthyroidism were further referred to a Baluchistan Institute of Child Health Services, Quetta for complete assessment and treatment. Those neonates with high, subclinical or borderline conditions were referred to a repeat test after 3-5 days, 15 days and 30 days after birth for reassessment and follow up. Data and test results of newborns were also entered in the well-designed questionnaire and entered on SPSS version 26.0 for further analysis through chi square test wherein the p value < 0.05 was considered as significant.

RESULTS

The majority of the pregnant hyperthyroid women were within the age group of 26-40 years with an overall mean age of 27.8±2.85 years. The present study results showed that majority of the pregnant hyperthyroid women were within the age group of 26-40 years with an overall mean age of 27.8±2.85 years. The clinical history presented previous still birth incidence in these women with a percentage value of 5.6%. There were only 38.2% of the women who did not receive the treatment for hyperthyroidism while majority in them were unidentified before (Table 1).

There were 87.6% those women who showed the presence of autoantibodies in them. The treatment percentage also elaborate the fact that there was a significant number of pregnant women either not treated or unknown of their condition. Majority of the treated pregnant women were taking combined carbimazole in combination with propylthiouracil (Table 2)

Within the delivered newborn there was no case reported of still birth or fetal abnormalities until the time of their discharge. However out of the total number of singleton deliveries there were 79.6% of the neonates born with normal body weight while 20.4% were found to be underweight. There was no significant within gender variance among cases (Table 3).

There were three neonates born with hyperthyroidism detected within the first 72 hours of their life. With treatment initiation two cases hyperthyroidism was brought under control and normalized while one child whose parents rejected for treatment suffered abnormal values of thyroid stimulating hormone even >30 days (Table 4).

The three infants who were suffering from congenital hyperthyroidism presented with typical symptoms of irritability, insomnia, insufficient body weight gain unless initiated with proper treatment plan. The detailed clinical assessment of the three congenital hyperthyroid neonate cases presented some common connection between all cases with unknown maternal TSH receptor antibodies and fetal variations. However, case # 3 had maximum gap between pregnancy and mother previous treatment as well as the similar case has lowest days of identification of its condition (Table 5). The overall incidence of congenital hyperthyroidism within pregnant women suffering from hyperthyroidism was reported as 0.6% with 0.4% those cases which were recovered through continuous treatment while 0.2% was that who was unrecovered due to treatment denial of parents/guardians (Fig. 1).

Table 1: Demographic and clinical features of hyperthyroid in pregnant women

Variable	Mean±SD	No. (%)
Age of mother (years)	27.8±2.85	500 (100%)
18-25	23.3±1.2	95 (19%)
26-40	31.3±4.5	405(81%)
Clinical birth History		
Fetal Abnormalities	----	25 (5%)
Fetal death/still birth	----	28 (5.6%)
Mother not received treatment	----	191 (38.2%)

Table 2: Biochemical characteristics and treatment received in pregnant women

Treatment Pattern in hyperthyroid women			
	Frequency (%)	CI (95%)	p value
Presence of Autoantibodies			
Yes	62 (12.4%)	46.6 (20.6-39.4)	0.043
No	438 (87.6%)	26.2 (22.0-30.4)	
Mother Received Treatment			
Yes	309(61.8%)	31.7 (23.5-39.9)	0.043
No	191 (38.2%)	21.4 (16.2-26.5)	
Type of Treatment			
Carbimazole Thyroxine	102 (20.5%)	29.4 (23.7-35.0)	<0.05
Propylthiouracil (PTU)	76 (15.2%)	25.8 (18.5-33.0)	
Combined Carbimazole and PTU	295 (59%)	21.6 (10.8-32.3)	
Thyroxine	27 (5.4%)	95.0 (11.2-178.7)	

Table 3: Weight distribution within the newborns

Newborn weight (grams)	Mean±SD	No. (%)	Gender
			Boy/Girl
Normal Weight (g)	2700±355	398 (79.6%)	120/200
Under Weight (g)	2200±98	102 (20.4%)	95/85

Table 4: Summary of maternal thyroid function tests and antibodies of newborns with overt hyperthyroidism

Case #	Gender	TSH (mIU/L				Treatment advised	Thyroid storm
		24-78 Hours	Day 3-5	Day 15	Day 30		
1	Boy	0.013	0.014	0.013	2.6	Yes	Yes
2	Girl	0.041	0.031	0.032	1.8	Yes	No
3	Boy	0.022	0.033	0.023	0.08	No	Yes

Table 5: Comparison of identified congenital hyperthyroid neonatal cases

Mother treatment	2.5 years prior	3 years prior	5 year prior
Maternal-TSH receptor-antibodies	Unknown	Unknown	Unknown
Fetal variations	Unknown	Unknown	Unknown
Gestational age in weeks	36	35	35
Weight; length at birth	2471g; 45cm	3010g; 47cm	2312; 46cm
Age at diagnosis	18 days	15 days	03 days
Diagnosis	Blood Spot Test	Blood spot test	Blood spot test

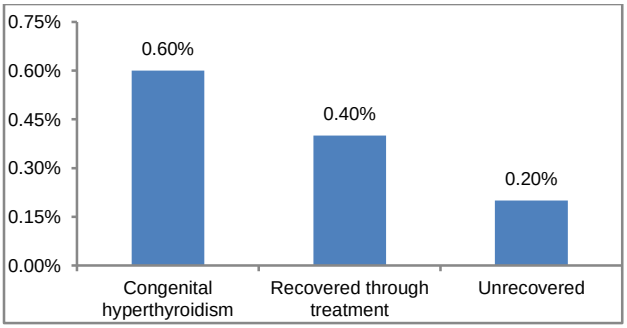

Fig. 1: Overall incidence of women suffering from hyperthyroidism

DISCUSSION

The incidence of congenital hyperthyroidism was found to be 0.6% among hyperthyroid pregnant mothers. The results of this study were in coordination with previously reported literature wherein the incidence of congenital hyperthyroidism in neonates was found to be 0.7%.[4] There are other studies which report the incidence much higher than the one reported in current study. A similar report was published by Dulek et al[5] wherein the incidence has been reported as 2.8%. The variance in the incidence rate may be caused by various genetic factors in different people all over the world.

The majority of the neonates had normal body weight which has been reported in other literature as well with similar findings.[12-14] Low birth weight is considered as a major concern which can lead to retardation and abnormal growth of the newborn. In Pakistan low birth weight is observed with a high percentage as 19% while in South Asia it has been recorded as 18.3%.[13]

In the present study there were 20.4% cases having low birth weight. The congenital hyperthyroid neonates were having low birth weight. Similar results have been reported earlier in other research studies.[15,16]

Within the three neonates born with congenital hyperthyroidism two of the cases suffered with thyroid storm. Out of these two cases the treatment of one neonate was started with Lugol's iodine, carbimazole and propranolol. The presence of anti-TPO/ anti-Tg is suggestive of autoimmune thyroiditis. Research elaborates that 10% of hyperthyroid mothers may also be tested positive with anti-TPO or anti-Tg. The Thyroid storm also termed as thyrotoxic crisis is an acute life-threatening condition which can be induced by excessive thyroid hormones. Early treatment can aid in saving life.[17-19]

The current study results showed that mother which is left untreated for long brings higher risk of congenital hyperthyroidism in their newborns. Among the various treatment plans for hyperthyroid mother carbimazole and propylthiouracil (PTU) were administered most for the used in the treatment of maternal hyperthyroidism. Carbimazole in combination with PTU are reported to be highly effective in monitoring and controlling the mother's hyperthyroidism.[20-23] It is pertinent to mention that PTU is linked with enhanced risk of liver injury, while carbimazole is associated with embryopathy.[24,25]

CONCLUSION

The overall incidence of congenital hyperthyroidism neonates within pregnant women suffering from hyperthyroidism was reported as 0.6%.

REFERENCES

1. Polak M, Le Gac I, Vuillard E, Guiboundenche J, Leger J, Toubert ME, et al. Fetal and neonatal thyroid function in relation to maternal Graves' disease. Best Pract Res Clin Endocrinol Metab 2004;18(2):289-302.
2. Wong SLJ, Jalaludin MY, Zaini AA, Samingan N, Harun F. Congenital hypothyroidism: An audit and study of different cord blood screening TSH values in a tertiary medical centre in Malaysia. Adv Endocrinol 2015;2015:387684.
3. Léger J. Management of fetal and neonatal Graves' disease. Horm Res Paediatr 2017;87(1):1-6.
4. Laurberg P, Andersen SL. Endocrinology in pregnancy: pregnancy and the incidence, diagnosing and therapy of Graves' disease. Eur J Endocrinol 2016;175(5):R219-30.
5. Dulek H, Vural F, Aka N, Zengin S. The prevalence of thyroid dysfunction and relationship with perinatal outcomes in the third trimester. North Clin Istanb 2019;6(3):267-72.
6. Lim BH, Raman S, Sivanesaratnam V, Ngan A. Thyrotoxicosis in pregnancy - a six year review. Singapor Med J 1989;30(6):539-41.
7. Deng F, Yang ZY, Zhang YP, Wang YL, Hu JY, Zhang F. TSH adenoma and syndrome of resistance to thyroid hormones - two cases report of syndrome of inappropriate secretion of thyrotropin. Brain Behav 2021;11(5):e02081.
8. Li C, Zhou J, Huang Z, Pan X, Leung W, Chen L, et al. The clinical value and variation of antithyroid antibodies during pregnancy. Dis Markers 2020;2020:8871951.
9. Chapman AK, Farmer ZJ, Mastrandrea LD, Matlock KA. Neonatal thyroid function and disorders. Clin Obstet Gynecol 2019;62(2):37387.
10. Papendieck P, Chiesa A, Prieto L, Gruñeiro-Papendieck L. Thyroid disorders of neonates born to mothers with Graves' disease. Pediatr Endocrinol Metab 2009;22(6):547-53.
11. Kahaly GJ, Bartalena L, Hegedüs L, Leenhardt L, Poppe K, Pearce SH. 2018 European Thyroid Association Guideline for the management of Graves' hyperthyroidism. Eur Thyroid J 2018;7(4):167-86.
12. Carmen MCT, Martín MJR, Ruiz JJ, Segura SA. Maternal autoimmune thyroid disease: Relevance for the newborn. Med Clin (Barc) 2015;144(7):297-303.
13. Wardlaw T, Blanc A, Zupan J, Åhman E. Low Birth weight: Country, Regional and Global Estimates. New York: UNICEF and WHO, 2004.
14. Levy-Shraga Y, Tamir-Hostovsky L, Boyko V, Lerner-Geva L, Pinhas-Hamiel O. Follow-up of newborns of mothers with Graves' disease. Thyroid 2014;24(6):1032-9.
15. Männistö T, Mendola P, Reddy U, Laughon SK. Neonatal outcomes and birth weight in pregnancies complicated by maternal thyroid disease. Am J Epidemiol 2013;178(5):731-40.
16. van der Kaay DCM, Wasserman JD, Palmert MR. Management of neonates born to mothers with Graves' disease. Pediatrics 2016;137(4): e20151878.
17. Miller A, Silver KD. Thyroid storm with multiorgan failure treated with plasma pheresis. Case Rep Endocrinol 2019;2019:2475843.
18. Samuels SL, Namoc SM, Bauer AJ. Neonatal thyrotoxicosis. Clin Perinatol 2018;45(1):31-40.
19. Lee ML, Wang YM, Chang MC. Concurrence of persistent pulmonary hypertension of the newborn, myocardial ischemia, supraventricular tachycardia, and congestive heart failure as a harbinger of neonatal Graves' disease. Acta Cardiol Sin 2020;36(3):272-5.
20. Banigé M, Polak M, Luton D, Research Group for Perinatal Dysthyroidism (RGPD) Study Group. Prediction of neonatal hyperthyroidism. J Pediatr 2018;197:249-254.e1.
21. Özon A, Tekin N, Şıklar Z, Gülcan H, Kara C, Taştekin A, et al. Neonatal effects of thyroid diseases in pregnancy and approach to the infant with increased TSH: Turkish Neonatal and Pediatric Endocrinology and Diabetes Societies consensus report. Turk Pediatri Ars 2018;53(Suppl 1): S209-23.
22. Besançon A, Beltrand J, Le Gac I, Luton D, Polak M. Management of neonates born to women with Graves' disease: a cohort study. Eur J Endocrinol 2014;170(6):855-62.
23. Taylor PN, Vaidya B. Side effects of anti-thyroid drugs and their impact on the choice of treatment for thyrotoxicosis in pregnancy. Eur Thyroid J 2012;1(3):176-85.
24. Rovelli R, Vigone MC, Giovanettoni C, Passoni A, Maina L, Corrias A, et al. Newborn of mothers affected by autoimmune thyroiditis: The importance of thyroid function monitoring in the first months of life. Ital J Pediatr 2010; 36:24.
25. Segni M. Neonatal hyperthyroidism. In: Feingold KR, Anawalt B, Boyce A, eds. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2019.

This article may be cited as: Kamal Z, Babar H, Mandokhel S: Incidences of Congenital Hyperthyroidism in Neonates Born to Hyperthyroid Women. Pak J Med Health Sci, 2023;17(12):281-283.