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Original Research Article

STUDY ON INCIDENCE OF CONGENITAL HYPOTHYROIDISM INTERMIN BORN NEONATES USING CORD BLOOD THYROID STIMULATING HORMONE LEVEL

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ABSTRACT

Background: To use cord blood TSH as a marker for screening of congenital hypothyroidismin term neonates.

Materials and Methods: It was a Prospective observational study. The study will be conducted on all term inborn delivered in hospital from over a period of 18 months from September 2020 to April 2022. The study was conducted at Department of Neonatology and Paediatrics, GEMS Medical College & Hospital, Srikakulam.

Results: A total of 625 study subjects out of which 53.1% (n=332) were female and 46.9% (n=293) were male subjects showing a female predominance. Out of 625 subjects 13 patients were suspected for congenital hypothyroidism. In our study 65.8% (n=411) mothers undergone Caesarean Section and 34.2% (n=214) have Normal Vaginal Delivery. Our study has revealed that the mean body weight of the studycases born was 2.89 kg ranging from 2.5kg to 3.3kg. The mean body weight in 68.96% (n=431) study subjects ranged between 2.51kg to 3.00kg, whereas, 31.04% (n=194) subjects weighed between 3.01-3.50 kg. In the suspected subjects the mean body weight is 2.79 kg ranging from 2.5kg to 3.3 kg. As far as maternal age is concerned it is noticed in our study that the mean age of all the mothers was 28.29 years, ranging from 21 years to 34 years, and the mean age of mothers of suspected patients is 29.54 years, ranging between 27 years to 32 years. The mean TSH at 3rd day after birth is noted to be 3.5 mU/L, ranging from 5 to 7.6 mU/L. As we have considered the cut of TSH value to be greater than 20 mU/L, our study resulted in 0/625 patients with congenital hypothyroidism.

Conclusions: To conclude, we can safely use a cut off of cord blood TSH value of>20 mU/L for the purpose of screening for congenital hypothyroidism. Large population-based studies are required to establish normative values for cord blood TSH in our country.

Keywords: TSH, Hypothyroidism, Body weight, Maternal Age, Congenital.

INTRODUCTION

Congenital hypothyroidism (CH) represents a heterogeneous group of thyroid disorders that manifests as thyroid hormone deficiency present at birth. It is most commonly caused by a problem with thyroid gland development or a disorder of thyroid hormone biosynthesis resulting in primary hypothyroidism whereas a deficiency of thyroid stimulating hormone (TSH) results in secondary or central hypothyroidism.[1,2] In India the prevalence has been reported to be 1 in 2640.[3]

Commonest causes of Permanent CH include thyroid dysgenesis probably due to inactivation of thyroid receptors maternal cytotoxic antibodies and genetic mutations lead to inactivation of thyroid receptors.[4] It affects 1 in 4000 live births. Secondly, synthetic defects in thyroid hormone accounting for 10% of all permanent CH cases. These disorders usually manifestasgoitrous hypothyroidism. Furthermore,

Permanent CH develops due to Iodine deficiency that is responsible for endemic cretinism and hypothyroidism in some regions of India. Lastly, hypothalamic- pituitary hypothyroidism that has an incidence of 1 in 100,000. It may be isolated or associated with concomitant deficiency of other pituitary hormones and present with hypoglycemia and microphallus.4

Congenital hypothyroidism is one of the more common preventable causes of mental retardation.[5,6] The clinical features of congenital hypothyroidism are often subtleand many newborn infants remain undiagnosed at birth.[7] The two main goals of the neonatal thyroid screening programme(NTS), early identification preferably within 1-2 months of birth and early adequate treatment, have been achieved to a great extent in the Western world. Unfortunately there is no such ongoing program, nor is there any detailed registry of congenital hypothyroidism patients in India.[8] This delay is also attributable to the lack of awareness about the illness, as well as the lack of facilities available or screening program in place to comprehensively screen and test newborns for this illness.[9]

Hence, in our study we studied the incidence of congenital hypothyroidism in term inborn neonates using cord blood thyroid stimulating hormone level.

Aims and Objectives

To use cordb lood TSH as amarker for screening of congenital hypothyroidismin term neonates.

MATERIAL AND METHODS

Study Design: Prospective observational study.

Study Area: Departmentof Neonatology and Paediatrics GEMS Medical College &Hospital, Srikakulam.

Study Population and Sample Size: The study will be conducted on all term inborn delivered in hospital from over a period of 18 months from September 2020 to April 2022.

The sample size is calculated as follows.

Previous,[10] studies were performed to evaluate the incidence of congenital hypothyroidism in term inborn neonates using cord blood TSH values. The incidence foundinthese articles ranges from5%to10%. Therefore, assuming(p)=7%with2% margin of error, the minimum required sample size at 5% level of significance is 625 patients.

Exclusion Criteria

1. Mother on any anti thyroid drugs
2. Preterm(<37wks)
3. Any major congenital anomaly
4. Critically ill neonates (on ventilator, inotropes, temperature instability, tachycardia (HR >160), Bradycardia (HR<95) (25), severe sepsis.
5. TSH Level<1mU/l(Central Hypothyroidism)

Inclusion Criteria

All term neonates delivered at Department of pediatrics, GEMS Medical College & Hospital, Srikakulam.

Methodology

This observational Study will be conducted in all term in born delivered in the hospital keeping the inclusion criteria in mind. Parent/guardian asked for permission of their children to participate in the study. After written &informed consent, detailed history were taken, physical examination was done, Umbilical (and if required, venous) blood sample is collected from the patients for investigations, and sent to the pathology department. Pre structured proforma used to record the details of patient at birth. For all term inborn neonates participating in the study, 2-3 ml of cord blood was collected in a sterile serum separating tubes (BD vaccutainer SST II advance) immediately after birth of babies, drawn from a 15-20 cm length of umbilical cord incised while severing it at the time of birth of the baby. Thus a mixed umbilical cord blood sample containing blood both from umbilical arteries and veins was obtained. Later, the Thyroid Stimulating Hormone values was determined by Electrochemiluminescence immuno assay method.

If the value of cord blood Thyroid Stimulating Hormone is>/= 20 mU/mL, thyroid profile of the baby shall be sent by peripheral venous sample between 3rd to 7th day of life, and if Thyroid Stimulating Hormone level is still >/= 20 mU/mL, it will be considered as congenital hypothyroidism.[54]

RESULTS

Table 1: Gender wise distribution of study subjects

Gender	Frequency	Percent
Female	332	53.1
Male	293	46.9
Total	625	100.0

Table 2: Maternal history wise distribution of study subjects

Maternal History	Frequency	Percent
Multiara	229	36.6
Primi	396	63.4
Total	625	100.0

Table 3: Mode of delivery wise distribution of study subjects

Mode of delivery	Frequency	Percent
CS	411	65.8

NVD	214	34.2
Total	625	100.0

Table 4: Mean of parameters of study subjects

Parameters	Minimum	Maximum	Mean	Std. Deviation
Bodyweight(Kgs)	2.5	3.3	2.89	1.43
Maternal age (Years)	21	34	28.29	2.90

Table 5: Mean TSH (mU/L) of study subjects at birth

Minimum	Maximum	Mean	Std. Deviation
2.30	61.00	8.07	4.57

Table 6: Gender wise distribution of suspected congenital hypothyroidism study subjects

Gender	Frequency	Percent
Female	5	38.5
Male	8	61.5
Total	13	100.0

Table 7: Mode of delivery wise distribution of suspected congenitalhy pothyroidism study subjects

Mode of delivery	Frequency	Percent
CS	6	46.2
NVD	7	53.8
Total	13	100.0

Table 8: Mean of parameters of suspected congenital hypothyroidism study subjects

Parameters	Minimum	Maximum	Mean	Std. Deviation
Body weight(Kgs)	2.5	3.3	2.79	0.26
Maternal age(Years)	27	32	29.54	1.98

Table 9: Comparison of mean TSH (mU/L) of suspected congenital hypothyroidism study subjects at birth and 3rd day follow-up

Time	Mean	Std. Deviation	t value	p value
At birth	30.5	12.2	7.928	<0.01*
After3days	3.5	0.9		

Table10: Mean TSH(mU/L) of suspected congenital hypothyroidism study subjects at 3rd day follow-up

Minimum	Maximum	Mean	Std. Deviation
5.0	7.6	5.92	0.65

Table11: Birth weight distribution of study subjects

Body Weight (Kg)	Frequency	Percent
2.51-3.00	431	68.96
3.01-3.50	194	31.04
Total	625	100.0

DISCUSSION

Congenital hypothyroidism (CH) signifies hypothyroidism present at birth and is one ofthe most common preventable causes of mental retardation.[11] It is now generally agreed that screeningof new borns for congenital hypothyroidism should be orientated to the detection of primary hypaothyroidism. This can be achieved by measurement of thyroxine in filter-paper blood spots, supplemented by TSH assay if the thyroxine concentration is found to be low. TSH screening program being the more sensitive of the two methods was disputed recently.[12] The successful introduction of screening in the 1970‘s has enabled North America, Europe, to a limited extent Asia, Latin America and a few African countries to combat the ill effects of CH and saved lives.[13]

Cord blood TSH has been found to be more sensitive than cord blood T4. Also it is considered to be easily available, accessible and simple.[47] In our study we evaluated the value of TSH in the newborn babies on the day of birth and then recalled and retested on3rdday to reconfirm the diagnosis and value of TSH into avoid false positive cases and know the actual incidence of congenital hypothyroidism.

In our study there were in total of 625 study subjects out of which 53.1% (n=332) were female and 46.9% (n=293) were male subjects showing a female predominance. The similar amount of studysubjects were taken in Ilamaran V et al 2014,[16] (n=785), Raj S et al 2014,[14] (n=430), Grant DB et al 198215(n=493).

Out of 625 subjects 13 patients were suspected for congenital hypothyroidism. The distribution showed 61.5 % male subjects (n=8) and 38.5 % female subjects (n=5). Other studies have also reported more male: female ratio such as Reddy JM et al 202117(n=17 M=9 F=8), Raj S et al 2014,[14] later stated the M:F ratio was 1:1.35. Some studies have reported no significant differences in the mean cord blood TSH level between males and females. These

studies include Ilamaran V et al 2014,[16] (males = 7.0±4.9mIU/L and females = 6.8±4.7m IU/L), Raj S et al 2014,[14] (p=0.814) and Gupta G et al 201418. Advanced maternal age and multiparity are high risk factors for birth defects multiparous mothers have high risk of genital tract infection, which may affect the environment and nutrition of embryo. With regard to maternal history, in our study 36.6% (n=229) were multipara and 63.4% (n=396) are primi. None of the studies reported such variations. In our study, when the maternal history was recorded in mothers with suspected patients it came out to be 5 multiparous mothers and 8 primiparous mothers.

In our study 65.8% (n=411) mothers undergone Caesarean Section and 34.2%(n=214) have Normal Vaginal Delivery. Several studies have investigated the effect of delivery type on the level of blood TSH, which has led to different results. In some works, higher prevalence of congenital hypothyroidism in neonates born with NVD is reported. On the other hand, there are some studies that claim that the prevalence of congenital hypothyroidism in neonates born with C/S is higher.[19,20] Raj S et al 2014,[14] found no correlation. On multivariate analysis requirement of resuscitation, mode of delivery and fetal distress as indication for lower segment cesarean section (LSCS) were found to be significant factors in a study by Gupta G et al 2014.[18]

13 patients, mothers of 46.2% (n=6) suspected patients has undergone Caesarean Section and 53.8% (n=7) mothers has undergone Normal Vaginal Delivery. The rationale behind this has not been well established, however it could be explained by stress events during pregnancy and labour. Our findings revealed that the presence of stress factors can result in an elevation in cord blood TSH.

Our study has revealed that the mean body weight of the study cases born was 2.89 kg ranging from 2.5kg to 3.3kg. The mean body weight in 68.96% (n=431) study subjects ranged between 2.51kg to 3.00kg, whereas, 31.04% (n=194) subjectsweighedbetween3.01-3.50 kg. In the suspected subjects the mean body weight is

2.79 kg ranging from 2.5kg to 3.3 kg. Many studies have shown almost same mean bodyweight for the babies born with congenital hypothyroidism including Raj S etal 2014,[14] (2.77kg).

As far as maternal age is concerned it is noticed in our study that the mean age of all the mothers was 28.29 years, ranging from 21 years to 34 years, and the mean age of mothers of suspected patients is 29.54 years, ranging between 27 years to 32 years. Some studies found a significant relationship with advanced maternal age and the incidence of congenital hypothyroidism including Rashmi Seth A et al 2007,[21] Kim EY et al 2005.[22]

ThemeanTSHvaluesfoundatthebirthwas8.07mU/MI ranging between 2.30 to 61.00 mU/MI as was depicted by several studies such as Gupta A et al 201418(1.01- 63.74 mU/L with median at 8.75).

Only 49 of the infants identified as being at risk were confirmed with subnormalblood T4 levels and clinical assessment as being hypothyroid. This gives a population incidence of 34/100 000 or 1: 2931 live births and a false positive diagnosis rate of 1.02% which is much higher than rates of 0.05–0.3% reported from other primary TSH screening programmes. Another study has shown that the population incidence of congenital hypothyroidism in Najran province of Saudi Arabia is 1:2931 live births. This rate is comparable to the incidence reported from other programmes in Saudi Arabia and elsewhere.[23]

In another study, incidence of CH is 0.29/1000 (1 in 3,400) which is close to worldwide incidence of 1 in 4,000. However, another study from South-Indian population reported incidence of CH as 1 in 1,700.88 The first ever study on prevalence reported that the high prevalence of dysmorphic features (94%), congenital heart disease (29%), and spina bifida occulta (41%) in our patients pointsto the fact that congenital hypothyroidism may not be an isolated event but rather a part of larger developmental syndrome resulting from some unknown insults during early embryogenesis. To our knowledge this is the first study ever to report the prevalence of dysmorphic features in this disease from India.

The postnatal surge in TSH levels, common to all newborns, is considered to be mediated through alpha adrenergic stimulation following the cold stress. In a study on neonatal rats, it was demonstrated that perinatal hypoxia increases the secretion of catecholamines. Similarly, a surge in catecholamine secretion was seen in human neonates during parturition; and this was more in asphyxiated newborns and in vaginally delivered newborns compared to those born by elective caesarean section. Others too observed that with perinatal hypoxia there is an increase in endogenous catecholamine, which is more pronounced when the scalp PH is less than 7.26. This alpha adrenergic stimulation in turn might be responsible for the observed increase in CB TSH in our subjects who had low Apgar scores, required active resuscitation after birth, were born through vaginal delivery or non-elective LSCS, and toprimiparous mother. However, in our study, no significant difference was found in CBTSH values in male and female neonates; nor any positive correlation found with the birth weight.

Various authors have correlated an increase in TSH values with factors like birth asphyxia and difficult deliveries, perinatal stress events, birth weight, male infant sex and instrumental delivery, and negatively with cesarean sections as mode of delivery but the mechanism are poorly understood.[18] Our figures have shown a comparable trend with the normative data for cord blood TSH values as reported by various workers across the globe.

CONCLUSION

Congenital hypothyroidism is the commonest preventable cause of intellectual impairment in

children. Incidence is 1:3000-4000 live birth around the World wide, while the estimated incidence is 1:1200-3400 live birth in Indian studies. Over the last two to three decades in all the developed and some of the developing countries. Mostly Specific features of congenital hypothyroidism are absent at birth which requires universal screening for early diagnosis and timely intervention. In our study we used cord blood TSH as a marker for screening of congenital hypothyroidism in term neonates. We evaluated the value of TSH in the newborn babies on the day of birth and then recalled and retested on 3rd day to reconfirm the diagnosis and value of TSH again to avoid false positive cases and know the actual incidence of congenital hypothyroidism. To conclude, we can safely use a cut off of cord blood TSH value of>20 mU/L for the purpose of screening for congenital hypothyroidism. Large population-based studies are required to establish normative values for cord blood TSH in our country.

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REFERENCES

1. Rastogi MV et al. Congenital hypothyroidism. Journal of Rare Diseases. 2010;5(17).
2. SujaPetal. Congenital hypothyroidism –Anusual suspectatanunusualage: A case series. Indian Journal of Endocrinology and Metabolism. 2013;17(1).
3. M P Desaiet al. Neonatal screening for congenital hypothyroidism using the filter paper thyroxine technique. Indian J Med Res. 1994.
4. Vandana J et al. Congenital Hypothyroidism. Indian Journal of Pediatrics. 2008;75(4):363-67.
5. Fisher DA et al. Second international conference on neonatal thyroid screening: Progress report. J Pediatr. 1983; 102:653-654.
6. Klein AH et al. Improved prognosis in congenital hypothyroidism treated before age three months. J Pediatr. 1972; 81:912-915.
7. LaFranchi S et al. Congenital Hypothyroidism: Etiologies, Diagnosis, and Management. Thyroid. 1999;9(7).
8. Reddy PA et al. High Prevalence of Associated Birth Defects in Congenital Hypothyroidism. International Journal of Pediatric Endocrinology. 2010; 940980:5 pages.
9. Unnikrishnan AG. Thyroid disorders in India: An epidemiological perspective. Indian Journal of Endocrinology and Metabolism. 2011;15(2).
10. Juraibah FA et al. Cord blood versus heel-stick sampling for measuring thyroid stimulating hormone for newborn screening of congenital hypothyroidism. Ann Saudi Med. 2019;39(5):291-294.
11. Alm J, Larsson A, Zetterstrom R: Congenital hypothyroidism in Sweden. Incidence and age at diagnosis. Acta PaediatrScand 1978, 67(1):1-3.
12. FisherD.A.SecondInternationalConferenceonNeonatalThyroidScreening: Progress report. J. Pediatr. 1983; 102: 653-4.
13. Delange F et al. Clinical aspects and systematic screening for congenital hypothyroidism in the newborn. Acta Paediatrica Belgica, 1977; suppl. VII, 30:3.
14. RajSetal.Cord Blood TSH LevelVariationsinNewborn – Experiencefrom A Rural Centre in Southern India. Journal of Clinical and Diagnostic Research. 2014; Vol-8(7):18-20.
15. Grant DB et al. Survey of neonatal screening for primary hypothyroidism in England, Wales and Northern Ireland 1982–4. BMJ 1988; 296:1355–8.
16. V. Ilamaran et al. Neonatal screening for congenital hypothyroidism using cord blood thyroid stimulating hormone. Curr Pediatr Res. 2014;18(2):76-78.
17. Reddy JM et al. Umbilical cord blood TSH level: correlation with congenital hypothyroidism. Int J Contemp Pediatr. 2021;8(7):1204-1208.
18. Gupta G et al. Cord blood thyroid stimulating hormone level-interpretation in light of perinatal factors Indian Pediatr. 2014;51(1):32-6.
19. McElduff A, McElduff P, Wiley V, Wilcken B (2005). Neonatal thyrotropin as measured in a congenital hypothyroidism screening program: influence of the mode of delivery. J Clin Endocrinol Metab, 90(12): 6361-3.
20. Soodejan MT et al. Trend of Congenital Hypothyroidism Incidence and Its Affecting Factors in Shahr-e-Kord, Western Iran. Iran J Public Health, Vol. 49, No.5, May 2020, pp.989-99.
21. Rashmi Seth A et al. Effect of perinatal factors on cord blood thyroid stimulating hormone levels. J Pediatr Endocrinol Metab. 2007;20:59- 64.
22. Kim EY et al. Perinatal factors affecting thyroid stimulating hormone (TSH) and thyroid hormone levels in cord blood. KoreanJPediatr. 2005; 48:143-47.
23. Bacchus R et al. Neonatal screening for congenital hypothyroidism in Riyadh. Saudi Med J 1988; 91:588–95.