IJCRR
Section: Healthcare
Sci. Journal Impact
Factor: 6.1 (2018)
ICV: 90.90 (2018)

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Newborn Screening for Congenital Hypothyroidism in Institutional Set Up in an Urban Area in Odisha

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ABSTRACT

Background: Congenital hypothyroidism (CH) is the most common preventable cause of mental retardation. Clinical manifestations of CH are not usually manifested at birth and remain undetected. The undetected CH infants show signs and symptoms of mental retardation at later age. Newborn screening for CH is a cheap and affordable tool to detect CH at birth to prevent mental retardation. There is the paucity of studies for detection of CH in this region of Odisha, hence this study.

Objective: To ascertain the incidence of CH in newborn babies and the effect of different variables on the level of TSH at birth.

Methods: This is retrospective observational study in babies born in selected centre of Odisha and newborns attending for a normal health check-up within 3-5 days. Estimation of TSH level from venous blood samples collected from 1530 neonates, included in this study, at 72-120 hours after birth and from 163 newborns, recalled for reestimation, at 21-30 days.

Results: Out of 1530 neonates, no case of CH was found. Incidence of CH was zero. However, different variants influenced the level of TSH. Level of TSH decreased with the advancement of age. Neonates with male sex, low birth weight and those born by vaginal delivery had a significantly higher TSH. Gestational age and parity did not affect TSH level. 163 neonates probably had Transitional Hypothyroidism.

Conclusion: CH can be detected at an affordable cost which outweighs the cost of investigation and treatment of CH and mental retardation in later life.

Key Words: Thyroid Stimulating Hormone (TSH), Newborn Screening (NBS), Congenital Hypothyroidism (CH).

INTRODUCTION

Congenital Hypothyroidism (CH) is the most common preventable cause of mental retardation.¹ The classical clinical symptoms and signs are usually not manifested in the vast majority of infants in their newborn period and gradually develop over a few weeks even in infants with thyroid agenesis.² Newborn screening (NBS) brought a revolutionary achievement in preventive medicine and showed a promising result. NBS for CH has been in practice in many developed countries since the early 1970s.³ Despite this, 71% of newborns worldwide have no access to the established NBS programme.⁴ During the past decades, several efficient NBS pilot studies for CH have established beyond doubt the need for a national NBS initiative.⁵ The Indian Academy of Pediatrics strongly advocated the inclusion of NBS in India's public

health policy.⁶ The Ministry of Health and Family Welfare Department of Govt. of India launched an NBS programme named "Rashtriya Bal Swasthya Karyakram (RBSK)" under the umbrella of National Rural Health Mission (NRHM)⁷, but this program is only in the infant stage and is not carried out at the peripheral level. Under these circumstances an attempt has been made to detect the incidence of congenital hypothyroidism in the urban health set up, to reach a definite diagnosis from the already ongoing procedure for future treatment modality.

MATERIALS AND METHODS

Two hospitals, one nursing home (where delivery is conducted) and one clinic, all non Government organizations,

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ISSN: 2231-2196 (Print)

ISSN: 0975-5241 (Online)

Received: 18.07.2020

Revised: 17.09.2020

Accepted: 12.11.2020

Published: 14.12.2020

situated in the geographical area of the Municipality participated in this study. The newborns in the local Govt. Community Health Centre was not included as NBS for CH is not done in this institution. All newborns delivered in these institutions and neonates, delivered at home and other institutions and attending the clinic for a routine check-up at 72-120 hours of life, irrespective of the mode of delivery i.e. normal vaginal or LSCS, gestational age, parity, birth weight was taken into the study. Total 1530 number of neonates were included in this study during a period from October 2018 to March 2020. Neonates, referred to higher institutions for ICU care were excluded.

The standard routing protocol, followed in these health institutions, is to collect venous blood samples for estimation of serum bilirubin at 72-96 hours of birth in two health institutions and 96-120 hours in one establishment. Therefore, the simultaneous estimation of thyroid-stimulating hormone was done from this venous blood sample. In the same way, an attempt was made to estimate TSH level from the venous blood samples meant for estimation of serum bilirubin drawn from neonates attending the private clinic at 72-120 hours of life. In India, majority of the screening programmes are conducted between 2nd and 5th day of birth to minimize false-positive high values (unless placental or cord blood is used) due to the physiological neonatal surge in TSH within 30 minutes of birth⁸. TSH testing was made by Sandwich Chemi Luminescent Immuno Assay Technique. The European Society for Pediatric Endocrinology (ESPE) Guideline (2014) was followed⁹ for treatment purpose as stated below;

- TSH ≥ 40 mIU/L of whole blood on DBS; start treatment immediately.
- TSH < 40 mIU/L of whole blood; Treatment can be a post-pond for 1-2 days to get Venous Sample Result.
- TSH > 20 mIU/L on Venous Sample requires Treatment, irrespective of FT4 levels.
- Low serum FT4 regardless of TSH level should be treated immediately.
- TSH of 6-20 mIU/L on Venous Sample with normal FT4 is a grey area; if TSH level remains high for 3-4 weeks or imaging results are suggestive of Thyroid Dysgenesis, treatment should be started immediately.

RESULTS

Total 1534 deliveries were conducted during the study period out of which 5 were twin deliveries. Out of 1539 newborns, 9 neonates were referred to a higher centre for complications and excluded from the study. Total 1530 number of neonates were taken into account. Newborn screening for thyroid was carried out and the serum level of TSH was estimated. Out of total 1530 newborns, TSH was estimated at 72-96 hours in 911 neonates and 96-120 hours in 619 neonates. The maximum TSH value was 16.56 and minimum was 0.01. Range

statistics, Mean and SD were 16.55, 3.4 and 2.3 respectively. We did not find a case of CH in our study.

Table 1 shows the trend of mean TSH value with the age of sampling. With the increasing age of sampling, there was a decline in the mean values. Impact of other variables on the TSH level was studied. Significant higher TSH values were noted in male babies, low birth weight neonates and neonates born by vaginal delivery (**Tables 2,3,4**). As the p-value was less than 0.001, all these variables had a significant correlation with TSH. The other two variables; gestational age and parity (**Tables 5,6**) had no impact on TSH level taking into consideration of p-value.

DISCUSSION

In our study of 1530 neonates, not a single case of CH was detected. Delange F reported the incidence of CH in an NBS programme to be 1:3000-1:4000 live births.¹⁰ Verma et al. reported the incidence of CH to be 1:1706 in a study in Delhi.¹¹ Agarwal et al in a study in 1998 found the incidence of CH to be 1:2640.¹² In a recent study conducted by the Indian Council of Medical Research (ICMR), screening several Inborn Metabolic Disorders between 2007-2012 in Delhi, Chennai, Hyderabad, Kolkata and Mumbai the overall incidence of CH was found to be 1:1130 newborns.⁵ In a study in Uttar Pradesh in India, Gopalkrishnan et al. in 2014 reported 11 cases of CH out of 13426 newborns screened, thus the incidence being 1:1221.¹³

We found significantly higher TSH values in low birth weight neonates, in male babies and in those born by vaginal delivery which is in agreement with other reports.¹³⁻¹⁵ However, further research is required to assess whether the association of higher TSH in low birth weight neonates explains the relationship between higher TSH and an adverse metabolic profile in later life.

We could not find any significant correlation between TSH value and gestational age which agrees with other reports.^{13,16-18} But in our view, the number of neonates of <37 weeks gestational age is too small i.e. 3.4% to arrive at a definite conclusion. Also, we noted that parity did not affect TSH values. The TSH level between primi and multi delivery (2nd or more) did not show any significant variation (p-value 0.685) which is similar to the reported data by SY Lee.¹⁹ Many studies have reported higher TSH levels in firstborn than subsequent neonates.^{14,20,21} Herbstman et al¹⁴ assumed this pattern to be related probably to environmental exposure where some persistent chemicals are present at higher levels in firstborn neonates. The relatively more stress and difficult labour associated with the first delivery in comparison to subsequent deliveries may increase TSH level. We found the diminishing value of TSH with the advancement of age which is in agreement with the data

reported previously.^{13,22,23} As expected, the later the sampling time, the lower the level of TSH in neonates.

Taking ESPE Guidelines into consideration, in the present study, 204 neonates who had TSH levels within the range of 6-20 mU/L, were re-called at 21 days after birth for estimation of TSH and 163 neonates reported at 21-30 days of life and all had TSH values within 6 mU/L, hence were declared as not having Congenital Hypothyroidism (CH). Probably these 163 neonates were cases of Transient Hypothyroidism.²⁴ Rest 41 neonates who didn't return for re-estimation of TSH were having TSH values between 6.0 to 7.1 mU/L and other 163 neonates had initial TSH levels within 7.0 to 16.56 mU/L. Though we could not find a single case of CH, (Table 7), we could establish that these 1530 newborns are not CH cases and hypothyroidism would not pose a threat of fatal neurodevelopmental consequences for them in later life.

Limitations of the Study

Our study had some potential limitations. The sample size was relatively small to arrive at a calculation of true prevalence. The data of Maternal TSH levels, Maternal anti-TSH receptor antibody and Urinary iodine levels which could have played an etiological role in case of transient CH were not available.

CONCLUSION

As stringent screening is not followed routinely in India, awareness among health care practitioners and parents regarding the benefit of early detection and treatment to prevent the adverse consequences of an easily and cheaply treated disease is highly warranted. Every available opportunity should be utilized at birth to estimate the TSH level from collected venous blood samples from healthy babies for any reason within the stipulated period. However, a large prospective study comprising of a sizable number of neonates from different parts of the state can throw a better idea on the incidence, prevalence and timely intervention of CH in the state.

ACKNOWLEDGEMENTS

GS conceived and planned the study. KB collected the data. PS wrote the manuscript. AS guided the study and did necessary rectification in the manuscript. Last but not the least, SM analysed the data and prepared the statistical analysis.

Financial support:- Nil.

Conflict of Interest:- Nil.

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Table 1: Mean screened TSH value mIU/L at various sampling age

Age of sampling	Number	Percentage of babies sampled	Mean	SD	p-value
72-96 hours	911	59.5	3.88	2.80	0.02
96-120 hours	619	40.5	2.78	1.13	

Table 2: Screened TSH levels as per sex

Sex	Number	Percentage	Mean	SD	p-value
Male	817	53.4	3.93	2.62	0.05
Female	713	46.6	2.87	1.81	

Table 3: Screened TSH levels as per birth weight

Parameter	Number	Percentage	Mean	SD	p-value
>2.5kg	1354	88.5	3.37	2.34	0.267
<2.5kg	176	11.5	3.99	2.28	

Table 4: Screened TSH levels as per the mode of delivery

Parameter	Number	Percentage	Mean	SD	P value
Vaginal	152	9.9	4.95	2.43	0.05
Caesarean	1378	90.1	3.27	2.27	

Table 5: Screened TSH levels as per gestational age

Parameter	Number	Percentage	Mean	SD	p-value
>37weeks	1478	96.6	3.44	2.35	0.749
<37weeks	52	3.4	3.33	2.15	

Table 6: Screened TSH levels as per parity

Parameter	Number	Percentage	Mean	SD	p-value
Primi	895	58.5	3.45	2.43	0.685
Multi	635	41.5	3.42	2.20	

Table 7: Recall for re-estimation of TSH

Parameter	No. of neonates
Initial TSH value 6-20mIU/L recalled at 21 days	204
Not reported	41
Reported at 21-30days	163
Final TSH value < 6mIU/L at 21-30days	163