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NEONATAL SCREENING FOR CONGENITAL HYPOTHYROIDISM AT BIMS HOSPITAL, BELAGAVI: ORIGINAL RESEARCH ARTICLE

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ABSTRACT

Background: Congenital Hypothyroidism (CH) is the most common preventable cause of mental retardation. To prevent the undesired developmental insults, newborn screening is needed which will be helpful to prevent serious disability. Aim of the study is to evaluate the prevalence of congenital hypothyroidism in babies born at BIMS Hospital, Belagavi. **Materials and Methods:** A total of 3420 term newborn babies were screened for Congenital hypothyroidism by a sample obtained by heel prick for a period of 2 years from May 2017 to May 2019. The 412 newborns with thyroid stimulating hormone (TSH) >10 mIU/L were re-examined. On 3rd – 7th day of birth serum TSH and thyroxin (FT4) levels were measured by CLIA method on Diasorin Analyzer from a venous sample. **Results and Conclusion:** Of 412 recalled subjects, 14 were confirmed to be hypothyroid, showing a prevalence of 4 in 1000 for CH. This is a hospital based small study showing high prevalence. Hence, there is a need of a study on screening program for a larger scale covering all quadrants of India equally.

KEYWORDS: Neonatal screening, congenital hypothyroidism, thyroid stimulating hormone.

INTRODUCTION

Congenital hypothyroidism (CH) is one of the most common congenital disorder. The prevalence of CH in newborns is 1/3000 to 1/4000.[1] This number may vary depending on the ethnicity, race, geographical distribution and the methods of screening newborns (i.e differences in sensitivity of diagnostic test).[2,3] CH occurs when a newborn is unable to

produce adequate thyroid hormone and if untreated, it may lead to serious impairment in mental and physical development.[4] CH is classified into 2 types, transient CH and permanent CH. Transient CH occurs due to temporary deficiency of thyroid hormone which later gets recovered in first few months of infancy. This occurs due to maternal and neonatal factors like antithyroid medications, antibodies blocking the transplacental thyrotropin, iodine deficiency or excess, congenital liver hemangiomas, very low birth weight baby (1500gm), premature baby (< 37 weeks of gestation) or thyroidal iodine organification defect.[5,6] Permanent CH occurs due to complete deficiency of thyroid hormone from birth and does not recover in later life.[5] Approximately 85% of the affected newborn are having permanent CH. The causes for permanent CH are thyroid dysgenesis including athyreosis, ectopic thyroid, hypoplastic thyroid, thyroid dyshormonogenesis or resistance to thyroid hormone, or because of abnormal transport of thyroid hormone.[7,8]

Neonatal screening is one of the major achievement in preventive medicine.[9] Neonatal thyroid screening is considered as a monitoring tool for the early detection and treatment of CH.[10,11] Most baby born with hypothroidism have normal apperance at birth and have no detectable physical or clinical signs of hypothyroidism. Data suggests that, on clinical diagnosis only 5% of the neonates are diagnosed as hypothyriodism; thus neonatal thyroid screening is essential for early diagnosis and helps in preventing mental retardation[12]. Also, the documentation of CH patients in India is very low.

Aim and objectives

To evaluate the prevalence of congenital hypothyroidism in babies born at BIMS Hospital, Belagavi.

Objectives

1) To determine the TSH levels from heel prick sample on Day 1 in all the babies born at BIMS Hospital.
2) To determine the TSH and FT4 levels from venous samples on Day 3 to Day 7 in babies with heel prick TSH level > 10 mIU/L.

MATERIALS AND METHODS

Study design:- It is a hospital based Cross sectional study.

S**etting:-** Department of Biochemistry at BIMS, Belagavi from May 2017 to May 2019

Participants:– All full-term newborn babies born at BIMS hospital, Belagavi.

Inclusion criteria:- Full term, normal vaginal delivery babies with birth weight ≥2.5kg were included in the study.

Exclusion criteria:- Low birth weight babies, preterm babies, babies born to hypothyroid mother or on antithyroid medications were excluded from the study. The study was approved from the institutional ethical committee and informed consent was taken from the mothers of all the newborns included in the study.

Biochemical analysis:- On day 1st the heel prick samples were collected from the newborns under strict aseptic conditions. The collected samples were analyzed for TSH levels in mIU/L. The newborns with TSH >10 mIU/L were re-examined. On 3rd – 7th day of birth the babies were re-called and the venous samples were collected. The collected samples were analyzed for serum TSH and thyroxin (FT4) levels by CLIA method on Diasorin Analyzer.

Statistical analysis

Data collected were entered in Microsoft Excel and SPSS Version 25 was used for analysis. The prevalence and incidence rate were calculated. A *p*-Value <0.005 was considered statistically significant.

RESULTS

A total of 3420 term newborn babies were screened for congenital hypothyroidism from May 2017 to May 2019. Out of 3420 newborn babies 412 showed high TSH value.

Screening protocol

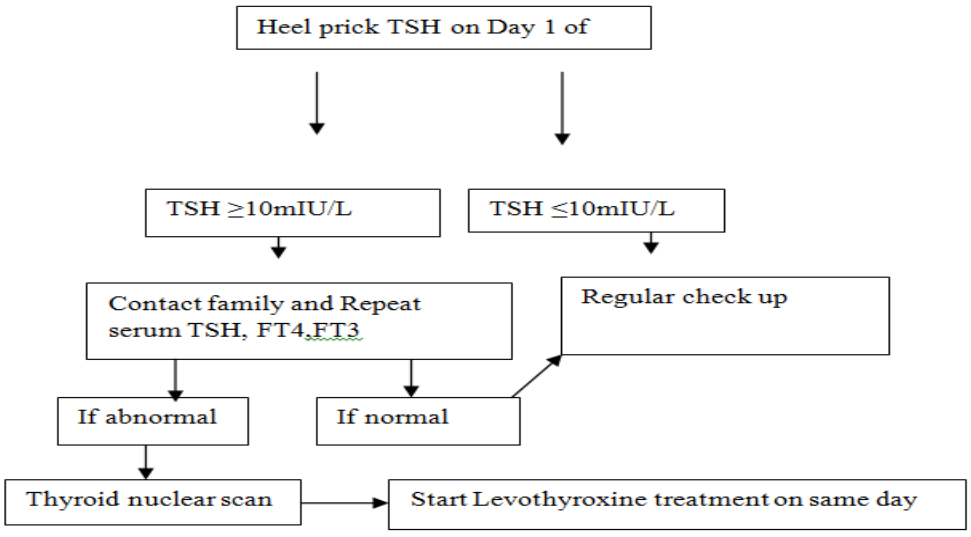

Figure 1: Frequency of newborns with high TSH levels from heel prick sample.

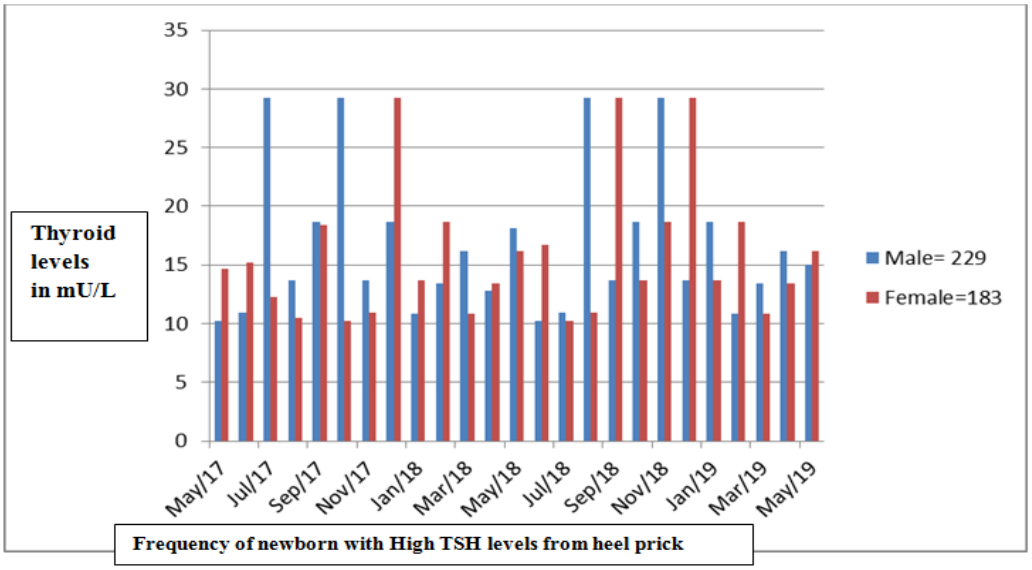

Figure 1 shows the newborn babies with high TSH levels from heel prick samples. Out of 412 babies with high TSH levels, 229 were male and 183 were female. The male to female ratio is 4:1.

Table 1: Genderwise distribution of babies with TSH >10mIU/L.

Total Babies with >10mIU/L	Male babies	Female Babies
412	229	183
Male-Female Ratio – 4:1		

Table 2: Newborns screened, Recall Rate and Prevalence of hypothyroidism.

Newborns screened	3420
Neonates with cord blood TSH >10mU/L	412
Recall rate*	12
Prevalence of hypothyroidism	4/1000 Newborns

*Recall rate= The neonates with cord blood TSH >10 mU/L per 100 screened neonates.

The babies with high TSH value were recalled again on 3rd to 7th day of birth and estimated for serum TSH and serum FT4 levels. In 412 subjects, 14 were confirmed to be hypothyroid. The prevalance of CH was 4/1000 babies born at BIMS Hospital, belagavi.

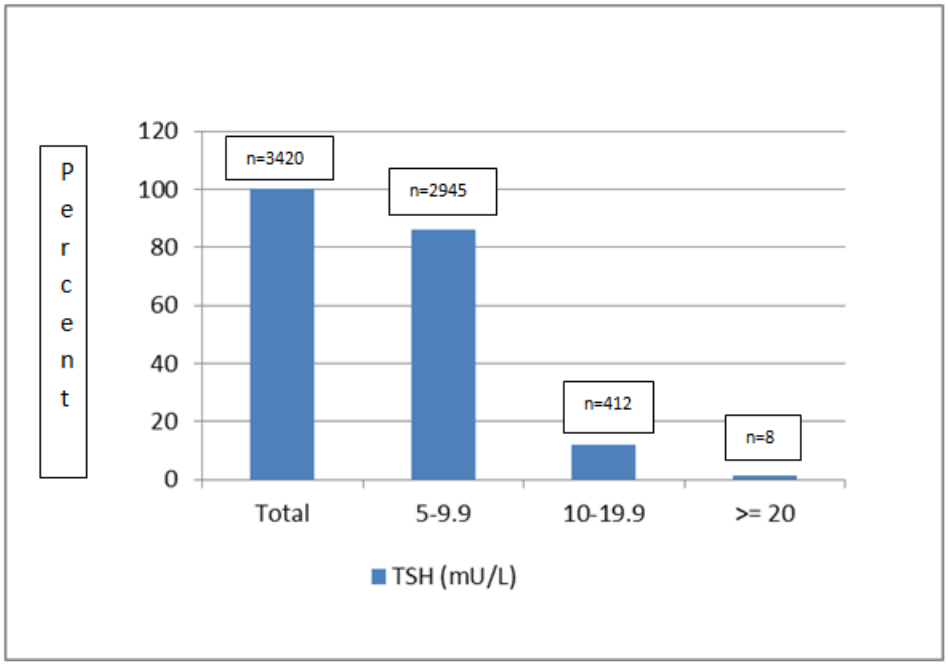

Figure 2: Frequency of neonates with cord blood TSH.

Figure 2 shows the frequency of neonates with TSH levels. 86.14% (n= 2945) of newborn have TSH levels between 5-9.9mU/L, 12.04% (n=412) of newborns have TSH levels between 10-19.9 mU/L and 1.23% (n=8) of newborns have TSH level >/= 20mU/L.

DISCUSSION

Over the past 20years, the incidence of CH appears to be increasing. This increase in prevalence is real or is it because of lowering the cutoff levels in screening tests is not yet clear.

In present study, the prevalence of CH was found as 4:1000 newborns considering heel prick TSH levels cutoff as 10mU/L. The prevalence found in present study is more compared to all the other studies.[13,14] The prevalence in more in males when compared to females with a ratio of 4:1 showing the male preponderance for CH. The cutoff TSH levels used in present study was > 10mU/L which has helped in eliminating a larger number of false positive and transient CH cases. The newborns included in study were all full term babies but still the prevalence rate is high. This could be because most of the women delivering in BIMS hospital come from a low socioeconomic background and with less literacy rate, who were unaware of there thyroid status before pregnancy. Also, the parents become more approachable to screening program only when they are having a congenitally diseased child or having repeated abortions or neonatal death.

The newborn screening allows the early identification and treatment of CH before clinical recognition. This has decreased the frequency of intellectually disabled childrens which was approximately 28% of affected newborns in pre- newborn screening era.[15] Thus, newborn screening programs for CH is very important and have been adopted since 1973 in almost all countries.[16] When the screening programmes were first started the cutoff of 20mU/L was considered. But during the course of time the cutoff is decreased to 10mU/L and this has increased the prevalence rates from 1:2441 to 1:1758 CH.[17]

In India the overall incidence of CH is 1:3000 to 1:4000 newborns with increased incidence in hispanic and asian individuals when compared to black individuals.[18] Desai et al[19] reported the prevalence of CH as 1:2640 in 1998.[19,13] Mengreli et al. also reported the prevalence of CH as 1:3384 in 2010[20] In Italy the prevalence was increased from 1:3200 to 1:2320 over a period of 10 years from 1987-2008.[21] Sanghvi and Diwakar found the incidence of CH as 2.1/1000 among term newborn babies, which was much higher than the incidence of 1/4000 reported in western literature and 1/1700 from other Indian literature.[22,23] A study from Hyderabad showed a prevalence of 1:1985 and 2.1:1000 from Kochi. Both these studies were hospital-based studies with relatively small sample sizes. In Uttar Pradesh the study was done by screening 1 lakhs neonates by ICMR and national task force team for a period of 2007-2012 and they reported a much higher prevalence of 1:1172 compared to all previous studies.

The probable reasons for the increased prevalence of CH in present study and other studies could be, improved testing strategies, decreasing the cutoff levels in screening test, increasing number of hospital delivery, increased awareness of screening programs and its benefits in the population, increasing number of preterm births, or it could be real and the actual incidence of CH is not being studied on a larger scale in the world's second largest populous country or there could be something else causing increase in incidence of CH. In addition, it is also not clear whether the newly detected cases of CH with mild hypothyroidism and delayed TSH rise will have transient hypothyroidism or permanent hypothyroidism.

The main causes for CH is thyroid dysgenesis (abnormal thyroid gland development) or dyshormonogenesis (disorder in synthesis of thyroid hormone) or due to deficiency of thyroid stimulating hormone (TSH) or due to defects in transport, action or metabolism of thyroid hormone. The common causes for thyroid dysgenesis are mutation in thyroid transcription factors (TTF-2) and mutation in gene encoding for transcription factors, which are important

in development of thyroid gland.[24] But in only 2% of CH cases thyroid dysgenesis are due to genetic mutations and 1/3rd of cases of CH occurs due to athyreosis (absence of thyroid gland) and hypoplasia of thyroid. Remining 15% of cases are due to dyshormonogenesis, or defect in peripheral thyroid hormone synthesis and transport.[25]

Thyroid hormone synthesis defects are familial in nature and usually inherited in autosomal recessive pattern.[26] These occur due to gene mutation of thyroid peroxide, sodium-iodide symport, generation of hydrogen peroxide, thyroglobulin, thyroid oxidase (THOX), dual oxidase (DUOXA), iodotyrosine deiodinase or defect in monocarboxylase transporter 8 or mutation in thyroid receptor. Most prevalent cause from above all causes is mutation in genes for thyroid peroxidase (TPO).[27]

Transient CH may be due to maternal thyrotropin receptor blocking antibodies, iodine deficiency or iodine excess or exposure of mother to antithyroid medications.

CONCLUSION

The present study shows the higher prevalence of CH (4:1000) when compared to all previous studies (1:1000 to 2.5:1000). All the studies mentioned above are done on a smaller scale and the results found cannot be generalized to whole population. So there is a need of a study on screening program for a larger scale covering all quadrants of India equally. Also, compulsory routine screening programs should be implemented in all health care systems. More support from the government is needed to make the neonatal screening more efficient.

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