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Research Article

Universal Newborn Screening for Congenital Hypothyroidism at a District-Level Tertiary Care Center in South India: A Prospective Observational Study

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ABSTRACT

Background: Congenital hypothyroidism (CH) is one of the main preventable conditions causing intellectual disabilities and delayed neurodevelopment in childhood. Although screening programs are established in several countries, district-level epidemiological data from India remain limited.

Subjects and Methods: This prospective observational study was conducted between September 2022 and February 2024 at a district-level tertiary care teaching hospital in South India. A total of 1551 consecutive live-born neonates underwent screening using heel-prick dried blood spot thyroid-stimulating hormone (TSH) estimation performed between 48 and 72 hours of life. Neonates with screening TSH values greater than 20 mIU/L were recalled for confirmatory venous thyroid function testing. Infants diagnosed with congenital hypothyroidism received levothyroxine therapy and were followed for six months.

Results: Among 1551 screened neonates, 18 infants (1.16%) had elevated screening TSH values and underwent confirmatory evaluation. Congenital hypothyroidism was confirmed in three infants, corresponding to an incidence of 0.19% (1:517 live births or 1.9 per 1000 live births; 95% confidence interval 0.4–5.6 per 1000 live births). All diagnosed infants started treatment within the first two weeks of life. Thyroid function was stable on medication, and there were no problems with development according to chronological age at six months' follow-up.

Conclusions: The results show that universal newborn screening resulted in a higher prevalence of CH among others when compared with a number of earlier regional reports. Early detection made it possible to start treatment promptly even without clinical symptoms. Thus, there is a possibility to expand newborn screening programs for all districts and regions.

Introduction

Congenital hypothyroidism (CH) is a common endocrine disease during the newborn period and still remains a major preventable cause of intellectual disability worldwide [1,2]. Thyroid hormones are involved in early brain development, neuronal migration, synaptogenesis and myelination during infancy (2,3). Delayed diagnosis and untreated hormone deficiency may thus lead to permanent neurodevelopmental impairment and growth failure.

Clinical diagnosis of congenital hypothyroidism in the neonatal period may be difficult, since many affected infants appear normal at birth. Residual thyroid activity and transplacental passage of maternal

thyroxine can temporarily conceal early manifestations of disease [4]. Therefore, diagnosis based on clinical examination alone may be delayed until clinical symptoms are present.

Dried blood spot thyroid-stimulating hormone estimation in universal newborn screening has dramatically improved the early detection of congenital hypothyroidism [1-5] in many countries. Infants diagnosed early and treated with levothyroxine in the first 2 weeks of life usually have better neurodevelopmental outcomes than infants diagnosed later [5,6].

India has one of the largest birth cohorts in the world, but the implementation of a national newborn screening program is not uniform. Epidemiological data are available mostly from urban tertiary care institutions with relatively limited district-level data [7,8]. Published studies from India have also shown variability in incidence between different geographic regions and populations.

Appropriate screening cutoff and recall systems for timely initiation of early treatment are important for improving screening effectiveness and minimizing false positive results [9-13].

Several international studies have additionally emphasized the importance of standardized screening protocols and long-term follow-up for optimizing developmental outcomes in affected infants [14–18].

The present study was undertaken to estimate the incidence of congenital hypothyroidism through universal newborn screening at a district-level tertiary care center in South India and to evaluate the early clinical and biochemical outcomes among affected infants.

Subjects and Methods

This prospective observational study was conducted at a district-level tertiary care teaching hospital in South India between September 2022 and February 2024. The institution caters to both urban and rural populations and conducts approximately 2500–3000 deliveries annually.

All consecutive live-born neonates delivered during the study period were included in the universal screening program. Stillbirths and neonates who died prior to sample collection were excluded from analysis.

Newborn screening for congenital hypothyroidism was performed using heel-prick dried blood spot samples collected between 48 and 72 hours after birth in order to minimize the influence of the physiological neonatal thyroid-stimulating hormone surge [9]. The same screening protocol was followed for term, preterm, and low-birth-weight neonates.

Thyroid-stimulating hormone estimation from dried blood spot samples was performed using time-resolved fluoroimmunoassay. A screening TSH value greater than 20 mIU/L was considered positive according to established national recommendations [10].

Neonates with abnormal screening results were recalled for confirmatory venous thyroid function testing. Confirmatory evaluation included serum thyroid-stimulating hormone and free thyroxine estimation using chemiluminescent immunoassay.

Congenital hypothyroidism was diagnosed when elevated serum thyroid-stimulating hormone levels were associated with reduced free thyroxine concentrations or when persistent thyroid dysfunction required initiation of treatment according to guideline-based recommendations [10].

Infants diagnosed with congenital hypothyroidism received oral levothyroxine therapy at a dose of 10–15 µg/kg/day. Treatment was initiated as early as possible, preferably within the first two weeks of life, to optimize neurodevelopmental outcomes [11].

Follow-up visits were conducted at 2 weeks, 1 month, 3 months, and 6 months after diagnosis. Clinical examination, anthropometric assessment, repeat thyroid function testing, and neurodevelopmental evaluation were performed during follow-up.

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages.

The incidence of congenital hypothyroidism was calculated as the number of confirmed cases among screened neonates, and exact binomial 95% confidence intervals were calculated [12].

The study was approved by the Institutional Ethics Committee of J.J.M. Medical College (Approval No: JJMMC/IEC-Syc-49-2022, dated 21 July 2022). Written informed consent was obtained from parents or legal guardians before participation. The study adhered to the principles of the Declaration of Helsinki and its later amendments.

Results

During the study period, a total of 1551 consecutive live-born neonates were universally screened for congenital hypothyroidism. Table 1 summarizes baseline demographic and perinatal characteristics.

Table 1: Demographic and Perinatal Characteristics of Screened Newborns (n = 1551)

Variable	Number (%)
Male	806 (52.0)
Female	745 (48.0)
Term births	1396 (90.0)
Preterm births	155 (10.0)
Vaginal delivery	838 (54.0)
Cesarean section	713 (46.0)
Mean birth weight (g)	2676.66 ± 414.06
Low birth weight (<2500 g)	197 (12.7)
Neonatal hyperbilirubinemia	546 (35.2)
Consanguinity	440 (28.4)
Maternal hypothyroidism	143 (9.2)

Of the neonates screened, 806 (52.0%) were males and 745 (48.0%) were females. Of the total deliveries, 1396 (90.0%) were term births and 155 (10.0%) were preterm neonates. Vaginal delivery was performed in 838 infants (54.0%) and 713 neonates (46.0%) were delivered by caesarean section.

The mean birth weight for the cohort was 2676.66±414.06 g. 197 neonates (12.7%) were of low birth weight (<2500 g). 546 (35.2%) infants had documented neonatal hyperbilirubinemia. Parental

consanguinity was reported in 440 (28.4%) cases and maternal hypothyroidism during pregnancy was observed in 143 (9.2%) mothers.

Initial dried blood spot thyroid-stimulating hormone screening identified 18 neonates (1.16%) with values >20 mIU/L. The recall rate was 100% as all screen-positive infants were successfully recalled for confirmatory testing (Table 2, Figure 1).

Table 2: Newborn Screening and Diagnostic Outcomes

Parameter	Value
Total newborns screened	1551
Screen-positive (TSH >20 mIU/L)	18 (1.16%)
Confirmed congenital hypothyroidism	3
False-positive screening results	15
Incidence of congenital hypothyroidism	1:517
Incidence (%)	0.19%
Incidence (per 1000 live births)	1.9
95% confidence interval (per 1000)	0.4–5.6

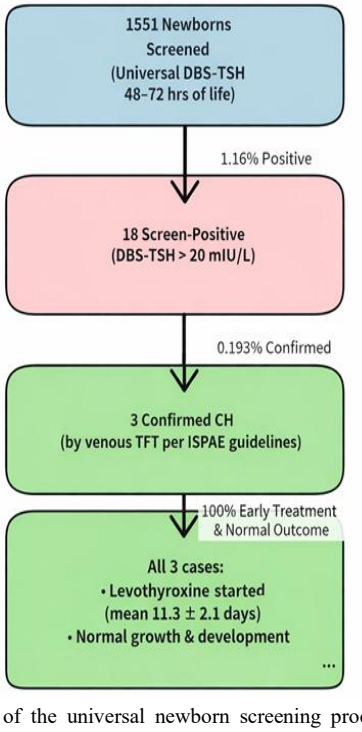

Figure 1: Flow diagram of the universal newborn screening process and outcomes for congenital hypothyroidism among 1551 newborns in Davangere district, Karnataka, India. DBS = dried blood spot; TFT = thyroid function test; CH = congenital hypothyroidism; ISPAE = Indian Society for Pediatric and Adolescent Endocrinology.

Three of these 18 neonates were confirmed to have congenital hypothyroidism and the remaining 15 infants had normal confirmatory thyroid profiles and were classified as false-positive screening results.

The overall incidence of congenital hypothyroidism in the current study was 0.19% (3/1551), which is 1 case per 517 live births or 1.9 cases per 1000 live births (95% confidence interval: 0.4–5.6 per 1000 live births) (Figure 2).

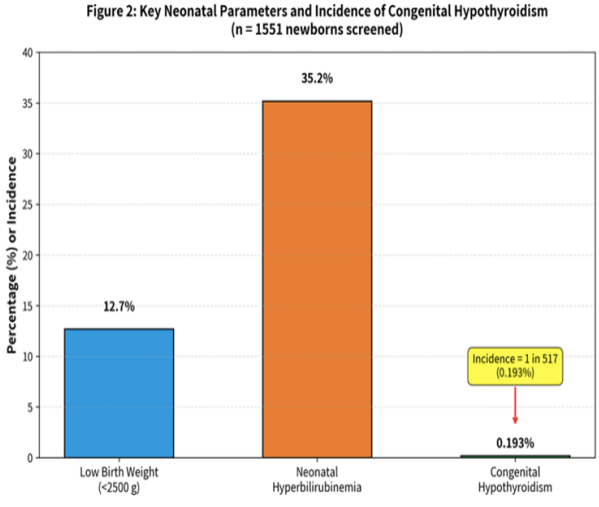

Figure 2: Prevalence of low birth weight (12.7%), neonatal hyperbilirubinemia (35.2%), and congenital hypothyroidism (0.19%; 1 in 517) among 1551 newborns screened in Davangere district.

All confirmed cases showed raised serum thyroid stimulating hormone levels in association with low free thyroxine levels consistent with primary congenital hypothyroidism. Two infants presented clinically with prolonged neonatal jaundice and lethargy, and one with no symptoms at diagnosis (Table 3).

Table 3: Clinical Characteristics of Infants with Confirmed Congenital Hypothyroidism (n = 3)

Variable	Case 1	Case 2	Case 3
Sex	Male	Male	Female
Gestational age	Term	Term	Term
Birth weight (g)	2600	2800	2700
Consanguinity	No	Yes	No
Initial symptoms	Jaundice	Lethargy	Asymptomatic
Age at diagnosis (days)	10	12	11

Levothyroxine therapy was initiated in all confirmed infants at doses ranging from 10–15 µg/kg/day. The mean age at treatment initiation was 11.3 days, and all infants started therapy within the first 14 days of life.

At six-month follow-up, thyroid function remained controlled on treatment in all infants. Growth parameters and developmental milestones were appropriate for age during follow-up assessment (Table 4). No infant was lost to follow-up during the study period.

Table 4: Treatment and Six-Month Follow-up Outcome

Variable	Case 1	Case 2	Case 3
Age at treatment initiation (days)	10	12	12
Levothyroxine dose (µg/kg/day)	10	12	10
Thyroid function at 6 months	Normal	Normal	Normal
Growth parameters	Appropriate	Appropriate	Appropriate
Neurodevelopment	Age-appropriate	Age-appropriate	Age-appropriate

Discussion

The present prospective study evaluated universal newborn screening for congenital hypothyroidism at a district-level tertiary care center in South India. The observed incidence of congenital hypothyroidism was 1:517 live births, which appears higher than several previously reported Indian and international estimates.

Earlier newborn screening programs from developed countries reported incidence rates ranging from approximately 1:3000 to 1:4000 live births. More recent studies, however, have demonstrated increasing incidence rates, partly related to improved screening sensitivity and modifications in screening cutoff values [13,14]. Indian studies have reported incidence rates ranging from 1:1700 to 1:3000 live births, although regional variation has been documented across different populations [14,15].

The relatively higher incidence identified in the present study may reflect improved detection through universal screening at the district level, where epidemiological data remain comparatively limited. The high prevalence of parental consanguinity observed in the present cohort may also have contributed to increased disease occurrence through genetic mechanisms such as dyshormonogenesis [16]. Environmental influences, iodine nutrition status, and regional genetic susceptibility may additionally influence the burden of congenital hypothyroidism despite universal salt iodization programs [17].

One clinically important observation in this study was that one infant diagnosed with congenital hypothyroidism remained asymptomatic during the neonatal period (Table 3). This finding emphasizes the limitations of relying solely on clinical examination for early diagnosis and highlights the importance of universal biochemical screening for timely identification of affected infants [18].

Early initiation of levothyroxine therapy remains one of the most important determinants of long-term neurodevelopmental outcome. Previous studies have demonstrated that treatment started within the first two weeks of life is associated with improved cognitive outcome and normal physical growth [13,19-20]. In the present study, all affected infants received therapy within this recommended therapeutic window and demonstrated satisfactory biochemical control along with age-appropriate growth and neurodevelopment during follow-up (Table 4).

The study has several strengths, including its prospective design, universal screening approach, complete recall of screen-positive neonates, and absence of loss to follow-up. In addition, it provides district-level epidemiological data from South India, where published information remains comparatively limited.

There are also some limitations that need to be discussed. For instance, this research took place only at one institution, and the number of patients identified as having a confirmed case was rather small, thus precluding subgroup analysis. Neither thyroid imaging nor genetic workup was done; thus, an etiological classification cannot be established. Additionally, the follow-up period lasted for only six months.

Conclusion

Universal newborn screening in the present study identified a relatively higher incidence of congenital hypothyroidism compared with several earlier regional reports. Screening using thyroid-stimulating hormone estimation enabled early detection of affected infants, including clinically asymptomatic cases, and facilitated timely initiation of levothyroxine therapy within the critical developmental period.

These findings support expansion of structured newborn screening services at district and national levels to improve early diagnosis and reduce congenital hypothyroidism-related neurodevelopmental morbidity.

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No funding was received for this study.

Conflict of Interest

The authors declare no conflict of interest.

Data availability

Data are available upon reasonable request.

Author Contributions

KPR contributed to conceptualization, data collection, and manuscript preparation; KLR contributed to study design, supervision, and manuscript review; MP contributed to data analysis, interpretation, and manuscript editing; RK contributed to conceptualization, critical revision of the manuscript, and final approval. All authors read and approved the final version, meet the ICMJE criteria for authorship, and agree to be accountable for all aspects of the work.

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