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Clinical Profile of Subclinical Hypothyroidism in Children Attending Tertiary Care Centre in Western India

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Abstract
To assess the clinical profile of subclinical hypothyroidism in children of 1-18 years of age at the time of presentation. The study was conducted among the children attending the paediatric and endocrinology departments of a tertiary care hospital at western India, (Gujarat). The statistical analysis was performed by IBM SPSS Statistics 20 version. Among the 40 children who were part of the study, the average age of presentation was 9.7 years. 45% of the children were males and 55% were females. The most common presenting symptoms were reduced physical activity (55%), weight gain (50%), constipation (50%), dry skin (50%) and poor scholastic performance (45%) and most common signs were pallor (55%) and delayed dentition (40%). Out of the 40 cases, 14 cases (35%) had a positive family history of thyroid disease in one of the parents and 1 case (2.5%) had family history of endocrine disease other than thyroid related disease running in the family. Among the anthropometric measures, 17.5% had short stature and 22% were overweight and 34% were obese. The normal range of TSH was taken as 0.5-5.0 mIU/L and all cases had TSH level above 5.0 mIU/L. In this study the mean TSH level was 6.86±8.4 mIU/L. Furthermore, thyroid antibodies were done in 19 cases out of which 7(36.8%) were elevated. USG thyroid was done in just 2 cases which showed diffuse glandular enlargement and focal nodule, respectively in each of the cases. Subclinical hypothyroidism affects growth and development of children. It is associated with various clinical manifestations and risk factors. Thyroid function tests and thyroid antibodies should be done in children with suggestive symptoms and signs. Early diagnosis and treatment may prevent complications and improve outcomes.

INTRODUCTION

Infants with very low birth weight (VLBW) constitute approximately 4-8% of live births., however, they account for roughly one-third of neonatal period deaths[1,2]. Birth weight (BW) and gestational age (GA) are critical determinants in predicting both the short-term and long-term quality of life of neonates. Neonates with low BW and GA exhibit a higher incidence of morbidity and mortality during the neonatal period. Furthermore, premature births are correlated with an elevated risk of mortality and morbidity[2-5].

Infants with very low birth weight (VLBW <1500 g) or those born at ≤32 weeks gestation represent a distinctive patient population within the neonatal intensive care unit (NICU). These VLBW infants, particularly those weighing <1000 g (extremely low birth weight [ELBW]), exhibit profound physiological immaturity. This immaturity renders them exceedingly sensitive to minor variations in respiratory management, blood pressure regulation, fluid administration, nutrition and virtually every other aspect of medical care.

The underdeveloped biological and physiological systems of these premature infants frequently result in a range of pathologies. These include respiratory distress syndrome (RDS), symptomatic patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), and broncho pulmonary dysplasia (BPD). Each of these conditions significantly impacts the prognosis of VLBW infants. In addition to these immediate health concerns, VLBW infants are also at a heightened risk for adverse neurodevelopmental outcomes. The combination of their physiological vulnerability and the complex medical challenges they face necessitates meticulous and specialized care to optimize both their short-term survival and long-term development[5-11].

The advancement of technology in NICU facilities, the availability of experienced and specialized NICU staff, the application of appropriate neonatal mechanical ventilation modes, surfactant therapy, and the introduction of antenatal and postnatal corticosteroid treatments have collectively increased the survival rates of neonates born with a birth weight of less than 1500 g to up-95%. However, these elevated survival rates have been accompanied by an increase in morbidity rates[11].

In this study, we aimed to determine the mortality and morbidity rates of VLBW infants or those born at ≤32 weeks gestation admitted to an NICU. Additionally, we explored the associated maternal risk factors.

MATERIALS AND METHODS

The study was conducted among children attending the Pediatric and Endocrinology departments of tertiary care hospital, Gujarat, India, from January 2022 to December 2022. Institutional ethics committee approval was obtained and informed consent was secured from the parents or guardians of the participants. Inclusion criteria encompassed children aged 1-18 years with serum TSH levels exceeding 5.0 mIU/L and normal free thyroxine (fT4) levels (0.8-1.8 ng/dL). Exclusion criteria included children with overt hypothyroidism, congenital hypothyroidism, thyroid hormone resistance, drug-induced hypothyroidism and other endocrine or systemic disorders that could influence thyroid function.

Data collected comprised demographic details, presenting complaints, family history of thyroid or endocrine diseases, anthropometric measurements (height, weight, body mass index and growth velocity), and clinical examination findings. Laboratory investigations included serum TSH, fT4, thyroid peroxidase antibodies (TPOAb) and thyroglobulin antibodies (TgAb). TSH and fT4 levels were determined using the electro chemiluminescence immunoassay (ECLIA) method with a Cobas e411 analyser (Roche Diagnostics, Mannheim, Germany). TPOAb and TgAb levels were assessed using the chemiluminescence immunoassay (CLIA) method with an Advia Centaur XP analyser (Siemens Healthcare Diagnostics, Tarrytown, NY, USA). The reference range for TPOAb was 0-34 IU/mL and for TgAb, it was 0-115 IU/mL. Thyroid gland ultrasonography (USG) was performed in selected cases.

Statistical analysis was conducted using IBM SPSS Statistics version 20. Descriptive statistics were employed to summarize the data. Mean and standard deviation were computed for continuous variables, while frequency and percentage were used for categorical variables. The chi-square test was applied for categorical variable comparisons, and the t-test was used for continuous variable comparisons. A $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSIONS

A total of 40 children with subclinical hypothyroidism (SCH) were included in the study. The mean age at presentation was 9.7±4.6 years, with a range from 1.5-18 years. Among the participants, 18 (45%) were male and 22 (55%) were female. The most frequently observed presenting symptoms were reduced physical activity (55%), weight gain (50%), constipation (50%), dry skin (50%) and poor scholastic performance (45%). The predominant clinical signs included pallor (55%) and delayed dentition (40%).

Table 1: Distribution of Symptoms

Symptoms	Frequency	Percentage
Lethargy	12	30%
Reduced physical activity	22	55%
Poor school performance	18	45%
Weight gain	20	50%
Dry skin	20	50%
Cold intolerance	6	15%
Constipation	20	50%
Delayed puberty	5	12.5%
Precocious puberty	2	5%

Detailed information on the symptoms and signs is presented in Table 1 and Fig. 1.

Among the 40 cases, 14 (35%) had a positive family history of thyroid disease in one parent, while 1 case (2.5%) had a family history of endocrine disorders unrelated to thyroid disease. Regarding anthropometric measurements, 17.5% of the children were identified as having short stature, 22% were classified as overweight, and 34% were categorized as obese. The reference range for thyroid-stimulating hormone (TSH) was set at 0.5-5.0 mIU/L., all cases exhibited TSH levels exceeding this range. The mean TSH level in this cohort was 6.86±8.4 mIU/L and the mean free T4 (fT4) level was 1.23±0.2 ng/dL. Thyroid antibodies were assessed in 19 cases, of which 7 (36.8%) displayed elevated levels. Thyroid ultrasonography (USG) was performed in 2 cases: one case showed diffuse glandular enlargement, while the other revealed a focal nodule.

Subclinical hypothyroidism (SCH) is a prevalent endocrine disorder in pediatric and adolescent populations, often remaining asymptomatic and detected incidentally during routine screening or evaluation of other conditions. However, some children may present with subtle or nonspecific symptoms indicative of hypothyroidism. In our study, common symptoms included reduced physical activity, weight gain, constipation, dry skin and poor scholastic performance, findings consistent with previous research[5,8]. Notably, pallor and delayed dentition were the predominant signs, aligning with reports from other studies[4,7]. These symptoms and signs suggest potential impairment of thyroid hormone action on various tissues and organs.

The etiology of SCH in children mirrors that of overt hypothyroidism, with autoimmune thyroiditis being the predominant cause. Other etiologies include iodine deficiency, congenital hypothyroidism, thyroid dysgenesis, thyroid hormone resistance and drug-induced hypothyroidism[6]. Our study identified a positive family history of thyroid disease in 35% of cases, suggesting a genetic predisposition. Additionally, elevated thyroid antibodies were observed in 36.8% of cases, indicating autoimmune thyroiditis, which is a known risk factor for the progression of SCH to overt hypothyroidism[10]. These findings are consistent with those of other studies[5,6]. Consequently, screening for thyroid antibodies and close monitoring of thyroid function in children with SCH is recommended.

The natural history of SCH in children is variable and influenced by factors such as age, sex, degree of TSH elevation, thyroid autoimmunity and environmental conditions[7]. Some studies report spontaneous normalization of TSH levels in 40-60% of cases, while others indicate progression to overt hypothyroidism in 10-30%[8,9]. Although our study did not include long-term follow-up, the mean TSH level was 6.86±8.4 mIU/L, which is relatively mild compared to other studies[11,12]. Higher TSH levels are associated with more severe symptoms and a higher risk of complications[13,14].

The management of SCH in children remains a topic of debate. There is no consensus on the optimal TSH cut-off values for diagnosis and treatment, the indications for levothyroxine therapy, or the long-term outcomes of untreated SCH[10]. Guidelines from the American Thyroid Association (ATA) and the European Thyroid Association (ETA) recommend an upper limit of normal TSH at 4.0 mIU/L for children and adolescents, except for those under two years of age, where it is 5.0 mIU/L. Levothyroxine treatment is advised for children with TSH levels exceeding 10 mIU/L, or those with TSH levels between 5.0 and 10.0 mIU/L if accompanied by thyroid antibodies, goiter, growth failure, or other hypothyroid symptoms[15,16]. For those with TSH levels below 10 mIU/L and without other treatment indications, monitoring every 6-12 months is recommended[15,16].

The efficacy of levothyroxine therapy for SCH in children is debated. Some studies report improvements in growth, lipid profiles, cardiac function, cognitive development and psychological well-being with treatment[11,13,18], while others find no significant differences compared to untreated cases[14-16]. Additionally, potential adverse effects of levothyroxine therapy include overtreatment, increased bone turnover and decreased bone mineral density[17,19]. Therefore, treatment decisions for SCH in children should be individualized, considering the balance of risks and benefits.

CONCLUSION

Subclinical hypothyroidism (SCH) is a prevalent endocrine disorder among pediatric and adolescent

populations, characterized by a range of clinical manifestations and associated risk factors. Thyroid function tests, along with the measurement of thyroid antibodies, are essential for evaluating children presenting with symptoms and signs suggestive of hypothyroidism. Prompt diagnosis and intervention may mitigate potential complications and enhance clinical outcomes. Further research is warranted to establish the optimal threshold for thyroid-stimulating hormone (TSH) levels, clarify the indications and efficacy of levothyroxine therapy and evaluate the long-term outcomes of untreated SCH in pediatric patients.

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