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Comorbidities of Thyroid Disease in Children

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Keywords

• Thyroid comorbidities • Pediatric thyroid disease • Hypothyroidism

Key points

- Thyroid disease even when treated results in mild persistent issues in cognition, weight, and mood in a subset of the population.
- Outcomes in congenital hypothyroidism are good but mild brain development issues are present in a subset of patients; growth is fine in nearly all treated patients.
- Prolonged hypothyroidism or hyperthyroidism impairs and alters growth outcomes even after the disease is identified and treated.

INTRODUCTION: COMORBIDITIES OF THYROID DISEASE IN CHILDREN

Thyroid disease in the pediatric population is routinely managed by pediatric endocrinologists. The management of thyroid disease is well established. However, as with diabetes in the pediatric population, because comorbidities have been assumed to not be of concern until adulthood, there is insufficient clinical and research attention devoted to examination of thyroid comorbidities in children.

This review article first covers hypothyroidism, with focus on congenital hypothyroidism (CH), acquired hypothyroidism, and subclinical hypothyroidism (SH). We conclude with a review of comorbidities of treated Graves' disease.

The focus of the article is largely on comorbidities that occur in patients even when they are identified and under medical care. We identify

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neurologic/psychiatric impact, growth effects, weight effects and related complications, and cardiovascular risk for each disease.

CONGENITAL HYPOTHYROIDISM

CH is most commonly caused by abnormal thyroid glandular development and includes agenesis, dysgenesis, and ectopic gland formation. Less common etiologies include dyshormonogenesis and transient CH secondary to transplacental passage of maternal medication, maternal blocking antibodies, or iodine deficiency or excess. Rarely, central hypothyroidism from pituitary or hypothalamic dysfunction is seen [1]. In the developed world, permanent primary CH affects approximately 1 in every 3500 live births [2]. Lower cutoff points for thyrotropin (TSH) levels have been incorporated in screening programs allowing for detection of mild forms of the disease, which has led to an increase in the reported incidence of CH [2].

Neurologic/psychiatric impact

Before the implementation of newborn screen programs, significant morbidity existed secondary to delayed or untreated CH. However, with implementation of newborn screen programs, nearly all children in the United States and the developing world are screened for CH and therapy with thyroxine is implemented within the first 3 weeks of life. For this reason, we do not focus on comorbidities seen as a consequence of lack of or significantly delayed initiation of treatment, primarily impaired neurocognitive development and overt cretinism, as such clinical scenarios are rarely encountered in today's practice, and are already well described [2–4].

Despite early initiation of treatment within the first 3 weeks of life, multiple studies have reported subtle deficits in cognitive and motor development in young children treated for CH after that time [1,2]. In a meta-analysis of studies comparing patients with CH with controls, a statistically significant impairment in motor development (primarily balance and fine motor skills) along with IQ deficit was seen among patients with CH. The most important risk factor was the severity of CH at diagnosis. The investigators concluded that some degree of impaired brain development in patients with CH may occur in utero and may not be prevented by early postnatal initiation of thyroxine treatment [5].

Impairment of verbal and memory functioning has also been noted among patients with CH despite early initiation of treatment [2,6]. Furthermore, based on MRI assessment, Wheeler and colleagues [6] noted that patients with CH showed compromised hippocampal development, an area of the brain essential for learning and memory.

The effect of different thyroxine replacement doses on intellectual development among patients with CH has also been evaluated with results suggesting that higher treatment doses of thyroxine result in improvement in IQ scores [7]. In one study, 83 patients with CH started on treatment between 21 to 25 days of life were divided into 3 groups based on starting treatment doses (6–8 μg/kg per day, 8.1–10 μg/kg per day, and 10.1–15 μg/kg per day). IQ was