J Pediatr (Rio J). 2017;xxx(xx):xxx–xxx

Jornal de Pediatria
www.jped.com.br

ORIGINAL ARTICLE

# Neonatal screening: 9% of children with filter paper thyroid-stimulating hormone levels between 5 and 10 μIU/mL have congenital hypothyroidism☆

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Received 10 October 2016; accepted 23 May 2017

**KEYWORDS**
Congenital hypothyroidism;
Neonatal screening;
Infant;
Newborn;
Thyroid diseases

**Abstract**
*Objectives:* To determine the prevalence of congenital hypothyroidism in children with filter paper thyroid-stimulating hormone levels between 5 and 10 μUI/mL in the neonatal screening.
*Methods:* This was a retrospective study including children screened from 2003 to 2010, with filter paper thyroid-stimulating hormone levels between 5 and 10 μIU/mL, who were followed-up during the first two years of life when there was no serum thyroid-stimulating hormone normalization. The diagnosis of congenital hypothyroidism was defined as serum thyroid-stimulating hormone ≥10 μIU/mL and start of levothyroxine treatment up to 2 years of age.
*Results:* Of the 380,741 live births, 3713 (1.04%) had filter paper thyroid-stimulating hormone levels between 5 and 10 μIU/mL and, of these, 339 (9.13%) had congenital hypothyroidism. Of these, 76.11% of the cases were diagnosed in the first three months of life and 7.96% between 1 and 2 years of age.
*Conclusion:* The study showed that 9.13% of the children with filter paper thyroid-stimulating hormone levels between 5 and 10 μIU/mL developed hypothyroidism and that in approximately one-quarter of them, the diagnosis was confirmed only after the third month of life. Based on these findings, the authors suggest the use of a 5 μIU/mL cutoff for filter paper thyroid-stimulating hormone levels and long-term follow-up of infants whose serum thyroid-stimulating hormone has not normalized to rule out congenital hypothyroidism.


☆ Please cite this article as: Christensen-Adad FC, Mendes-dos-Santos CT, Goto MM, Sewaybricker LE, D'Souza-Li LF, Guerra-Junior G, et al. Neonatal screening: 9% of children with filter paper TSH levels between 5 and 10 μIU/mL have congenital hypothyroidism. J Pediatr (Rio J). 2017. http://dx.doi.org/10.1016/j.jped.2017.05.003
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http://dx.doi.org/10.1016/j.jped.2017.05.003

**PALAVRAS-CHAVE**
Hipotireoidismo congênito;
Triagem neonatal;
Lactente;
Recém-nascido;
Doenças da glândula tireoide

## Triagem neonatal: 9% das crianças com tsh em papel filtro entre 5 e 10 μUI/mL têm hipotireoidismo congênito

### Resumo

*Objetivos:* Determinar a prevalência de hipotireoidismo congênito em crianças com TSH em papel filtro (TSH-f) entre 5 e 10 μUI/mL na triagem neonatal.

*Métodos:* Estudo retrospectivo incluindo crianças triadas de 2003 a 2010, com TSH-f entre 5 e 10 μUI/mL, que foram acompanhadas nos dois primeiros anos de vida quando não houve normalização do TSH sérico. O diagnóstico de hipotireoidismo congênito foi definido como TSH sérico igual ou superior a 10 μUI/mL e início de tratamento com levotiroxina até os dois anos de idade.

*Resultados:* Dos 380.741 nascidos vivos triados, 3.713 (1,04%) apresentaram TSH-f entre 5 e 10 μUI/mL e, destes, 339 (9,13%) tinham hipotireoidismo congênito. Destes, 76,11% dos casos foram diagnosticados nos primeiros três meses de vida e 7,96% entre um e dois anos de idade.

*Conclusão:* O estudo mostra que 9,13% das crianças com TSH-f entre 5 e 10 μUI/mL desenvolveram hipotireoidismo e que em cerca de um quarto delas o diagnóstico só se confirmou após o terceiro mês de vida. Com base nestes achados, sugere-se a utilização do ponto de corte de TSH-f de 5 μUI/mL e o acompanhamento em longo prazo dos lactentes cujo TSH sérico não tenha se normalizado para descartar o hipotireoidismo congênito.



## Introduction

Congenital hypothyroidism (CH), the most frequent congenital endocrine disorder and one of the main causes of preventable intellectual disability with early diagnosis and adequate treatment, was one of the first diseases screened in neonatal screening (NS) programs.[1–4]

The incidence of CH before the creation of NS programs was estimated at 1:6500,[5] but soon after the start of NS programs, it increased to approximately 1:3000 to 1:4000 live births (LB).[6] In recent years, there has been a further increase in CH incidence in several parts of the world, ranging from 1:1030 to 1:2679 LB.[7–10] This fact is probably associated with an increase in the survival of preterm newborns,[4,7] environmental[11] and ethnic factors,[7] as well as the reduction in the cutoff values of thyroid-stimulating hormone (TSH) on filter paper (f-TSH) in NS programs.[4,12]

Initially, higher f-TSH cutoff values were adopted to avoid recalls and excessive costs, with the justification that mild forms of CH would have no consequences for the neurological development.[4] However, some authors suggested that there were insufficient studies to support this hypothesis,[4] and the European Consensus on Congenital Hypothyroidism of 2014 highlighted, as the primary objective of NS, the detection of all cases of primary CH.[1]

In recent years, several screening services have chosen to lower the cutoff value of f-TSH to reduce the number of cases of undiagnosed CH.[4,13–17]

With this reduction, several programs reported an increase in the number of children diagnosed with CH through NS programs,[4,13–17] although there has also been an increase in the number of children with suspected CH and, therefore, a higher rate of recall.[4,15,16,18]

Since 2001, the Neonatal Screening Program of Universidade Estadual de Campinas (UNICAMP) has used a cutoff of 5 μIU/mL for f-TSH and has performed clinical and laboratory follow-up for at least the first two years of life of all children whose serum TSH levels do not normalize.

Considering this context, the aim of the present study was to determine the prevalence of CH in children with f-TSH levels between 5 and 10 μIU/mL in the NS.

## Methods

### Neonatal screening strategy for congenital hypothyroidism

UNICAMP'S Neonatal Screening Reference Service (Serviço de Referência em Triagem Neonatal [SRTN]) is currently responsible for neonatal screening, diagnosis, and comprehensive care of children in the VII (Campinas) and XIV (São João da Boa Vista) Regional Health Departments, regions that have approximately 5000 LB per month.

Since its creation, UNICAMP SRTN has worked with the same team for the treatment and follow-up of the cases, and the laboratory and imaging investigations have always been performed at the services of UNICAMP hospital complex.

UNICAMP SRTN uses the cutoff value for f-TSH of 5 μIU/mL in a dried whole-blood sample on filter paper, equivalent to 11 μIU/mL in serum, and the analyses are performed by time-resolved fluorometry (AutoDELFIA–Perkin Elmer Life Sciences, MA, USA).

UNICAMP SRTN uses the following protocol for the diagnosis and treatment of CH: children with f-TSH >5 μIU/mL or ≤0.01 μIU/mL are called in for serum TSH and free thyroxine (T4L) measurement. If serum TSH and T4L levels are normal, the children are discharged from the service. Children with serum TSH values higher than the reference values for age, but lower than 10 μIU/mL, are monitored through clinical