

INITIAL VERSUS CONFIRMATORY THYROID STIMULATING HORMONE (TSH) LEVELS: IS THERE A CORRELATION?

Sylvia Capistrano-Estrada, Kahlil Izza T dela Cruz, Carmencita Padilla

Institute of Human Genetics, National Institutes of Health, University of the Philippines Manila

Abstract. Newborn screening for congenital hypothyroidism (CH) in the Philippines began in 1996. The screening method used is the fluoroimmunoassay of thyroid stimulating hormone (TSH) from dried blood spot. In the past five years (June 1996 - Sept 2001), 176,548 newborns have been screened. Of these, 237 had elevated TSH levels and 51 (22%) were confirmed to have CH. One hundred forty-six (61%) had normal TSH levels on confirmatory testing; five (2%) expired; 25 (11%) were lost to follow-up, while 10 (4%) were being recalled at the time of this study. Thirty-three out of 51 (65%) CH patients are female. Only 38 of 51 patient charts were available for data analysis. Thirteen of 51 CH patients were lost to follow-up after confirmation of the disorder. The mean age at which levo-thyroxine was initiated is 1½ months at a modal dosage of 25 µg OD. The initial TSH levels as determined by the Philippine Newborn Screening Laboratory directly correlates with the confirmatory TSH levels done in other endocrine laboratories (Spearman's rho=0.57, p value=0.0002, at a=0.05). However, the time of heel prick on the newborn was independent of the TSH levels, (Spearman's rho=-0.16, p value=0.377 at a=0.05) hence there was no significant difference with respect to the initial TSH level of blood samples taken at 48 hours, less than one week, one to two weeks; or even more than two weeks after birth (Kruskall Wallis test, p value=0.064 at a=0.05). Using Fisher's exact test, there is no sufficient evidence to say that there is an association between gender and the incidence of CH among screened newborns whose TSH levels were initially elevated (p 2-tailed=0.183, p 1-tailed=0.113 at a=0.05).

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders in childhood. During the past decades, newborn screening for congenital hypothyroidism has become an important health activity in most developed countries. These screening programs have not only benefited patients and their families but also produced new information about the epidemiology, pathophysiology, diagnosis, and treatment of thyroid disease in infancy and childhood (Vela *et al*, 1999). Newborn screening for congenital hypothyroidism in the Philippines began in 1996 and has so far detected 51 newborns with congenital hypothyroidism, having a prevalence of 1:3,748 (Newborn Screening, 2001).

The Philippine Newborn Screening Program measures primary TSH or thyroid stimulating hormone as a means of screening newborns for congenital hypothyroidism. Majority of European and Japanese programs favor screening by means of this method, supplemented by T4 determinations for those infants with elevated TSH values (American Academy of Pediatrics, 1987). Newer TSH assay techniques, such as the enzyme-linked immunoassays, chemiluminescent

assays, and fluoroimmunoassays, offer the advantages of using non-radioactive labels and greater sensitivity with the potential for better separation between normal and abnormal TSH concentrations. Thus, many screening programs are considering switching to a primary TSH approach (American Academy of Pediatrics, 1987).

OBJECTIVES

This study aimed to determine if there is a correlation between the time of heel prick and initial TSH levels; a correlation between the initial TSH levels determined on the newborn screening card and the confirmatory plasma TSH levels determined by other endocrine laboratories; and to determine if there is an association between gender and susceptibility to CH among newborns whose screening TSH levels were elevated.

MATERIALS AND METHODS

All confirmed cases of primary congenital hypothyroidism in the newborn screening laboratory were identified. Retrospective chart review was done. The following were obtained: sex, birth date, age when heel prick was done, date of screening, initial TSH value

obtained from NBS laboratory, confirmatory TSH, age at which levo-thyroxine was initiated, and the initial dosage. The confirmatory TSH levels were converted to mIU/ml, the standard unit used by the Philippine NBS laboratory in measuring initial TSH levels. Spearman rank correlation at a significance level of 0.05 ($\alpha = 0.05$), Fisher's exact, and Kruskal Wallis Test were used for statistical analysis.

RESULTS AND DISCUSSION

During the past five years, a total of 176,548 newborns were screened. Of these, 237 newborns had elevated initial TSH levels. Fifty-one patients (22%) were confirmed to have CH while more than half (61% or 146 newborns) of them turned out to have normal TSH levels on the confirmatory testing, five (2%) expired, twenty five (11%) were lost to follow-up, while ten (4%) were still being recalled (Fig 1). Out of 51 CH patients, 18 (35%) of these were male (Table 1). However, two of these only had transient CH.

The mean age at which levo-thyroxine medication
 Table 1. Gender Distribution versus Incidence of congenital hypothyroidism among newborns with elevated initial TSH levels.

	Positive for CH	Negative for CH
Male	18	64
Female	33	82
Total	51	146

was prescribed is 1.5 months at a modal dosage of 25 μg OD. Two-tailed spearman rank correlation at $\alpha = 0.05$ was done to determine whether initial TSH level and confirmatory TSH value are statistically independent of one another. A Spearman's rho value = 0.57 ($p = 0.0002$) was obtained, suggesting that there was a direct relationship between initial TSH and confirmatory TSH. Among the 237 screened newborns who initially yielded elevated TSH levels, about 22% (51 patients) were confirmed positive for CH, more than half of whom were female (33 newborns).

The high percentage of false positive results can be attributed to the normal occurrence of high TSH levels among newborns, thereby the need for confirmation by measuring plasma FT4 and TSH. Fisher's exact test at $\alpha = 0.05$ between gender and incidence of CH among screened newborns whose TSH levels were elevated showed that statistically, there was no association between gender and incidence of CH, although it may seem that the incidence in females was far higher than in males (P value two-tailed = 0.183, p value one-tailed = 0.113). There was no significant correlation between the age of the newborn at the time of heel prick and the initial TSH values (Spearman's rho = -0.16 $p > /t/ = 0.3770$). Moreover, there was no significant difference with respect to the initial TSH level of blood sample taken at 48 hours; less than one week; one to two weeks; or even more than two weeks after birth (Kruskall Wallis test, P value = 0.064 at $\alpha = 0.05$).

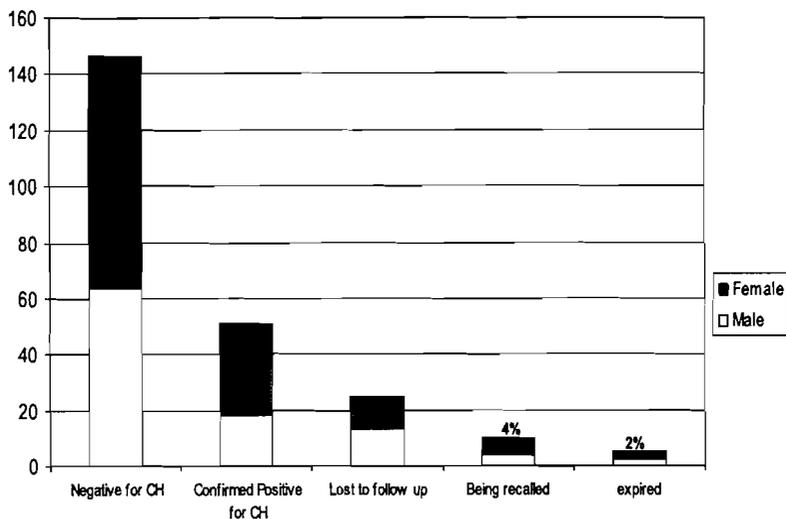


Fig 1. Distribution of 237 screened newborns with elevated initial Thyroid Stimulating Hormone Levels.

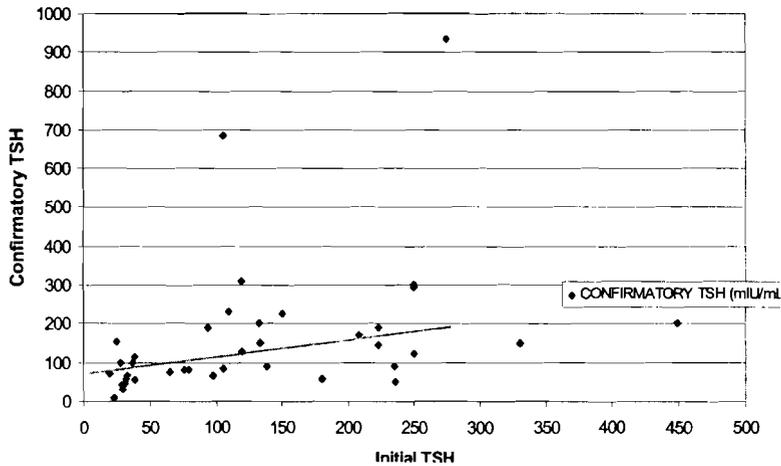
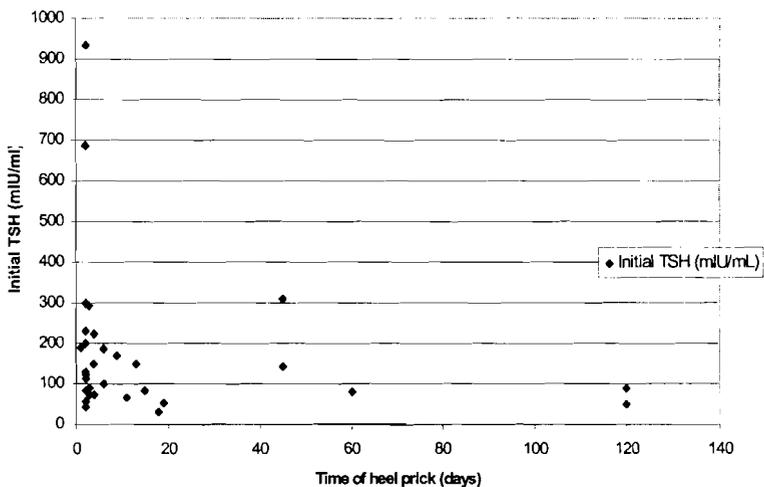


Fig 2. Correlation between initial TSH and Confirmatory TSH values.



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Vela M, Gamboa S, Loera-Luna A, Aguirre BE, Perez-Palacios G, Velazquez A. Neonatal screening for congenital hypothyroidism in Mexico: experience, obstacles, and strategies. *J Med Screening* 1999; 6:77-9.