Original Article

# Correlation Between Congenital Hypothyroidism and Hearing Loss in Newborn

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## Abstract

**Introduction:** Congenital hypothyroidism increases the risk of hearing loss which caused delay speech and language development, social and emotional problems, and educational failure. Currently, a universal hearing screening program in newborns has been implemented in Thailand. The congenital hypothyroidism is not considered as a risk factor for hearing loss resulting in restricted hospitals that do not be screening hearing loss among congenital hypothyroidism. Then this research is to study the correlation between congenital hypo-thyroidism and hearing loss in a newborn in Uttaradit hospital, Thailand.

**Methods:** A retrospective cohort study of 382 newborns in Uttaradit hospital between January 2011 to June 2020 was obtained from medical records, Thyroid-stimulating hormone (TSH) screening report in newborn, the evaluation of otoacoustic emission (OAE) and auditory brainstem response (ABR), divided into 2 groups, 62 patients were congenital hypothyroidism (exposed group) and 320 patients were non-congenital hypothyroidism (non-exposed group). Data were analyzed by using descriptive statistics and analytical statistics by a computer program.

**Results:** Newborn with congenital hypothyroidism was 2.5 times significantly greater risk of hearing loss (95% CI 1.27 - 4.95, $P = .008$).

**Conclusions:** Congenital hypothyroidism affected hearing loss in newborns. Therefore, early screening should be necessary for newborns to reduce the risk of hearing loss and also improve the quality of life.


**Keywords:** Correlation, Congenital hypothyroidism, Hearing loss, Newborn

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## Introduction

Congenital hypothyroidism (CH) is inadequate thyroid hormone production at birth.[1] Thyroid hormone is an important factor for the development of the fetal ear and auditory function.[2] Auditory impairment is reported frequently in relation to congenital hypothyroidism more explicitly than acquired hypothyroidism.[3]

CH is one of the most common endocrine pathology in childhood with a worldwide incidence of 1:3,000 to 1:4,000 which closes to the incidence in Thailand.[1,4-5] The prevalence of hearing loss among CH childhood was estimated by Chulalongkorn hospital, Thailand in 2018 at approximately 20%.[6,7] Hearing loss in infants caused delay speech, language development, social, emotional problems, and education failure. Therefore, hearing loss in newborn should be early screening and appropriate intervention particularly in the first 6 months of age.[8]

Currently, a universal hearing loss screening program has been implemented in high-risk groups in Thailand due to limited health care personnel and resource. Restricted hospitals may be screening in a high-risk group.[9] Nevertheless, CH is not considered as a risk factor for hearing loss by the Joint Committee on Infant hearing loss[10] so restricted hospitals do not be screening hearing loss among CH.

Therefore, the study of the relationship of CH and hearing loss is necessary to aware of the risk and promote congenital hypothyroidism to hearing loss and early deserved hearing loss screening test in newborn. To effectively protect the occurrence of hearing loss. The objective is to study the correlation between congenital hypothyroidism and hearing loss in a newborn in Uttaradit hospital.

## Methods

**Study design:** etiologic research, retrospective cohort study

**Population:** 25,405 newborns in Uttaradit hospital with TSH screening were reported from January 2011 to June 2020. Sample Size estimation was computed by STATA program version 12.1E which using power = .80 and alpha = 0.05. 382 newborns were enrolled in this study and divided into 2 groups: the exposed group (62 cases) and non-exposed group (320 cases) which using ratio 1:5.

**Inclusion criteria:** newborns in Uttaradit hospital with TSH screening report

**Exclusion criteria:** newborns in Uttaradit hospital with atresia or stenosis of the external ear canal

Statistic for data analyzed:

1. Descriptive statistic

1.1 Categorical data are analyzed as amount and percentage. The compare proportion test to evaluate across different groups by chi-square and Fisher's exact test. The null hypothesis for the difference in proportion across groups in the population is set to zero.

1.2 Continuous data are analyzed as mean and standard deviation. The compare the means of two groups by t-test or Wilcoxon rank-sum test.

2. Analytical statistic

2.1 Univariate risk regression analysis interpreted as Risk ratio, 95% CI and *P*-value by using .05 Significance level.

2.2 Multivariate risk regression analysis interpreted as Risk ratio, 95% CI and *P*-value by using .05 Significance level.

## Results

Table 1 provides general characteristic was analysis from 320 newborns in Uttaradit hospital of whom 62 newborns in the exposed group and 320 newborns in the non-exposed group. 211 in males (65.9%) and 109 in females. Exposed groups are birth weight ≥ 2500 grams (79.0%) gestational age more than 36 weeks (84.2%), maternal age 20 - 35 years old during labor (83.3%) maternal history about thyroid hormone disease (19.7%) history of received ototoxic drug in newborn (89.4%) no history of sepsis (95.7%) means of TSH screening is 29.53 mu/L (46.58%) mean of TSH at diagnosis is 20.4 (27.1%) and mean of free T4 at diagnosis is 1.4 (0.8%).

**Table 1** Characteristics of study subjects

| Characteristics | Congenital hypothyroidism | | Non Congenital hypothyroidism | | *P*-value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| **Gender** | | | | | |
| **Male** | 40 | 64.2 | 171 | 53.4 | .108 |
| **Female** | 22 | 35.5 | 149 | 46.6 | |
| **Birth weight (g)** | | | | | |
| **< 2,500** | 13 | 21.0 | 56 | 17.8 | 560 |
| **≥ 2,500** | 49 | 79.0 | 258 | 82.2 | |
| **Gestational age (Week)** | | | | | |
| **< 36** | 6 | 15.8 | 32 | 11.0 | .415* |
| **≥ 36** | 32 | 84.2 | 260 | 89.0 | |
| **APGAR at 5 minutes** | | | | | |
| **Normal (> 6)** | 59 | 100 | 302 | 97.4 | .365* |
| **Abnormal (≤ 6)** | 0 | 0 | 8 | 2.6 | |
| **Maternal age (Year)** | | | | | |
| **< 20** | 1 | 1.9 | 46 | 45.7 | .024 |
| **20 - 35** | 45 | 83.3 | 208 | 71.0 | |
| **> 35** | 8 | 14.8 | 39 | 13.3 | |
| **Maternal history of thyroid hormone disease** | | | | | |
| **Yes** | 12 | 19.7 | 2 | 0.6 | < .001 |
| **No** | 49 | 80.3 | 309 | 99.4 | |
| **Sepsis** | | | | | |
| **Yes** | 6 | 10.2 | 42 | 13.5 | .485 |
| **No** | 53 | 89.8 | 269 | 86.5 | |
| **Ototoxic** | | | | | |
| **Yes** | 11 | 18.64 | 103 | 33.0 | .028 |
| **No** | 48 | 81.4 | 209 | 67.0 | |
| **TSH screening(mU/L) Mean (Standard deviation)** | 29.5 (46.6) | | 5.4 (3.8) | | < .001* |
| **TSH at diagnosis(mU/L) Mean (Standard deviation)** | 20.4 (27.1) | | | | |
| **FT4 at diagnosis(ng/dL) Mean (Standard deviation)** | 1.4 (0.8) | | | | |

Abbreviations: TSH, Thyroid-stimulating hormone; FT4, Free thyroxine; APGAR, Activity Pulse Grimace Appearance and Respiration

Congenital hypothyroidism with hearing loss patients was 19.4% and non-congenital hypothyroid with hearing loss patients were 9.69%. Percentage of 2 groups were statistically significant differences at the significant level of .028 is shown in Table 2.

**Table 2** Hearing loss between 2 groups

| Characteristics | Congenital hypothyroidism | | Non congenital hypothyroidism | | *P*-value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| **Hearing loss** | 12 | 19.4 | 31 | 9.7 | .028* |
| **Normal** | 50 | 50 | 289 | 90.3 | |

The risk ratio of hearing loss patients with congenital hypothyroidism had 2 folds increased risk of developing hearing loss (95% CI 1.02 - 3.90, $P$ = .042). Likewise, the ototoxic drug exposured patients have increased the risk of 2.37 folds (95% CI 1.28 - 4.37, $P$ = .006). Meanwhile, hearing loss patients with sepsis increased the risk of 3.11 folds (95% CI 1.61 - 6.01, $P$ = .001) is shown in Table 3.

**Table 3** Univariable risk regression of the hearing loss

| Characteristics | Risk ratio | 95% CI | *P*-value |
|---|---|---|---|
| **Congenital hypothyroidism** | 2.00 | 1.09 - 3.67 | .0286 |
| **Ototoxic** | 2.37 | 1.34 - 4.19 | .003 |
| **Sepsis** | 3.11 | 1.74 - 5.58 | .0007 |

Abbreviations: CI, confidence interval

After analysis by log risk regression, patients with congenital hypothyroidism are 2.5 folds increased the risk of developing hearing loss of without congenital hypothyroidism at 95% confidence interval 1.26 - 4.94 and significant level of .008 is shown in Table 4.

**Table 4** Multiivariable risk regression of the hearing loss

| Risk ratio | Risk ratio | 95% CI | *P*-value |
|---|---|---|---|
| **Congenital hypothyroidism** | 2.50 | 1.27 - 4.95 | .008 |
| **Ototoxic** | 1.88 | 0.88 - 4.02 | .103 |
| **Sepsis** | 2.15 | 0.89 - 4.83 | .062 |

Abbreviations: CI, confidence interval

## Discussion

The results showed 19.4% of hearing loss in the exposed group is close to reporting in general populations.[11] Related to research in Taiwan, showing 25% of congenital hypothyroidism with hearing loss. Also, related to a study in Canada that found 20% of hearing loss in congenital hypothyroidism. However, the percentage of hearing loss in congenital hypothyroidism is not related to research in Qazvin, in the study of Northern India has no one was hearing loss from congenital hypothyroidism.[12] In the non-exposed group had percentage closed to the research of Rawish Kumar is 9.7%[28] and research in Iran.[11]

There was a statistically significant difference in the percentage of hearing loss among those with and without congenital hypothyroidism is not related to research in Iran.[11] The percentage of hearing loss were different due to types of hearing screening test, age during a hearing screening, ethnic and genetic factors.[5]

From a univariable risk regression analysis study, the factors which significantly increase the risk are congenital hypothyroidism, ototoxic exposure and sepsis which are related to American,[13] African,[14] and northern Thailand research.[15] The research of Vohr et al., discovered the most frequent high-risk factors for hearing loss are ototoxic exposure 44.4%.[16] And 41.3% from Roi-Et hospital.[17] Ototoxic drugs have the potential to cause cellular damage in the inner ear, leading to vestibular and cochlear function losses.[18] Research in mice of Schmutzhard and Fischer reported that sepsis leads to a significant hearing loss due to apoptosis of supporting cells of the organ of Corti and can change in the inner hair cell and spiral ligament.[19, 20]

The factors that need to be studied were disturbed by external variables, therefore should be considered to external variables by Multivariate risk regression analysis from log risk regression and control other variables. It is found that ototoxic exposure and sepsis are not statistically significant risk factors of hearing loss which related to research in Germany[21] but not related to other previous researches. Congenital hypothyroidism has significantly increased the risk of hearing loss which is related to the previous study. (1) In the animal study, exhibit that the thyroid hormone plays role in the development of the inner ear.[5] The absence of thyroid hormone during the end of pregnancy and early childhood can cause irreversible hearing loss in both humans and rodents.[22] (2) In congenital hypothyroidism affect to development and function of the ear, the important period of ear development is from the embryo to the first-year of life. Normally the thyroid gland will begin in 11 - 12 weeks of gestation, result in remain dependent on maternal thyroid hormone via the placenta until the fetal thyroid gland can produce thyroid hormone at 16 - 20 weeks of gestation. Consequenctly congenital hypothyroidism occurs during a critical period leads to hearing loss.[3] (3) Thyroid hormone, especially T3, is important for inner ear development. Thyroid hormone deficiency causes impaired maturation of cochlea epithelium then obstructed potassium channels in which necessary for propagating an auditory signal and causes poorly developed of outer hair cell in the tectorial membrane if not received to sufficient thyroid hormone.[23] (4) Congenital hypothyroidism induced fetus results underdeveloped the sensory epithelium of the inner ear, with periods necessary to thyroid hormones for the cochlear development.[24]

Hearing loss from congenital hypothyroidism has a chance to return to normal hearing if given T4 before the first year of life.[3] In a previous research, appropriate hormone replacement can improve hearing loss or return to normal hearing.[25] Karakus's research found L-thyroxine replacement after 4 months will improve the hearing condition.[26] In Egypt research recommended that hormone replacement therapy should be continued for at least 6 months to achieve a condition of euthyroid state.[27] However, the best prevention should start hearing screening from birth and follow up regularly until childhood.

For this research analyzes the specific correlation between congenital hypothyroidism and hearing loss in the newborn as a small study in Thailand and this research methodology is a retrospective cohort study, which appropriates for rare incident and can reduce bias in determining the correlation of risk factor and outcome.

The results of the study are inconsistent with the research results above due to the retrospective cohort study design may cause incomplete obtained data. In addition, the worldwide incidence of hearing loss in congenital hypothyroidism is only 1.7 per 1,000. Also, the incidence of congenital hypothyroidism approximately 1:3,000 to 1:4,000 is close to the incidence in Thailand. As a result, there are not enough populations to study and data from the first Otoacoustic emission (OAE) report are available but the hearing loss can occur later. For the next study, the population groups should be enlarged and prospective cohort study design together with conducted hearing screening reports from follow-up appointments and certain diagnoses for complete data, reduce data error and add an appropriate sample size. The conclusion from the study is shown congenital hypothyroidism was a risk for hearing loss in statistical significance.

Therefore, congenital hypothyroidism should be considered as a risk for hearing screening in newborn to early appropriate treatment and constantly monitor the hearing screening for the prevention of hearing loss in the future and to enhance people's quality of life.

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