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Hearing Deficit in Children with Congenital Hypothyroidism

Esraa Majid Mutashar*[1], Munib Ahmed Alzubaidi[2]

[1,2,] *Children Welfare Teaching Hospital – Medical city / Baghdad*

*Corresponding Author , contact email : esraamajid75@gmail.com

Original Article

Summary

Primary congenital hypothyroidism is a common endocrine disease & remains the leading cause of preventable mental impairment worldwide. Children with congenital hypothyroidism can develop hearing problems as part of extrathyroidal comorbidities of congenital hypothyroidism. Thyroid hormones are crucial for auditory pathways development and maturation. However, the incidence of hearing loss is still uncertain, and it could affect about 20% of patients with congenital hypothyroidism. This study aimed to assess prevalence and type of hearing loss in children with congenital hypothyroidism and its association with presence or absence of thyroid gland. Therefore, this cross-sectional study was conducted on patients diagnosed tohave congenital hypothyroidism (primary). All patients were followed up at the department of pediatric endocrinology of the Children Welfare Teaching Hospital – Medical city / Baghdad. The study included 67 children aged one week to 16 years. Hearing acuity was assessed in all congenital hypothyroid patientsusing methods based on the age of the child. Findings revealed that congenital hypothyroidism was more frequent in children at age 1-5 years Female to male ratio was 1.09 to one. Hearing impairment found infive (7.5%) patients of sensorineural type & in the frequency ranges of moderate, severe & profound. The association of hearing deficit & thyroid agenesis was not significant. In conclusion, Children with congenital hypothyroidism have to be carefully followed and their hearing acuity should be monitored and evaluated regularly .

Keywords: *Congenital Hypothyroidism, Deafness, Hearing Impairment*

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1. INTRODUCTION

Congenital disorder of thyroid gland in children are not uncommon, however, congenital hypothyroidism (CH) is the most frequent one. Globally, it represents the leading cause of preventable mental disorders. Deficient Iodine or thyroid dysgenesis are the most common cause of CH. Also CH can be due to disorders in the regulation , production or function of thyroid hormones (1). CH affects approximately 1:4000 live births. It is more common in girls with a male to female ratio of 2:1. (2). The disease is based on a complete or partial insufficiency of thyroid hormones, leading to a delay in the development of many organs, as well as to irreversible changes in the child's nervous system. The syndrome of congenital hypothyroidism is a heterogeneous group of diseases in terms of etiology. In the vast majority of cases (up to 90%), primary congenital hypothyroidism occurs, in which the process leading to a lack of synthesis of thyroid hormones is localized directly in the thyroid gland. The most common is primary hypothyroidism caused by thyroid dysgenesis (agenesis, hypogenesis, dystopia). Another reason for the decrease in the synthesis of thyroid hormones is a violation of hormone genesis in the thyroid gland itself. These are the lack of the ability to concentrate iodide, a violation of iodine organization (dysfunction). Because even severe hypothyroidism is usually clinically silent in newborns, neonatal blood testing is usually recommended. Screening samples should be taken from all infants prior to hospital discharge, ideally between 2 and 4 days of age, to avoid the rise in TSH levels associated with normal neonatal TSH surge (3). In recent decades, unusually high rates of congenital extrathyroidal comorbidities have been reported in newborns with CH. However, published data varies considerably from country to other and in different ethnic groups. (4) The prevalence of congenital defects in the general population is only 3%, approximately 10% of patients with CH (5). Most of them were cardiac. (6) However, approximately 20% will have neuro-sensory hearing defects. (7) abnormalities of nerves, kidneys, and eye have also been documented (8). The major role for thyroid hormone is in the morphogenesis and developmental maturation of auditory process. So that, a potential risk factor of hearing deficit is the CH (9). The effect of T3 on cochlear sensory cells is due in part to differential expression of TH receptor isoforms. The receptors in the developing cochlea are α (THRA)

& β (THRB). (10) Insufficient formation of microtubule stability can also be verified: changes with a higher expression of fibrin-actin, which increases the rigidity - shrinks the cell membrane. These changes affect the cochlear amplification process. (11) SLC26A4 gene expression may also be reduced in patients with hypothyroidism. This gene encodes a protein that acts as a motor for outer hair cells and regulates the cochlear amplification process. (12) Reduces the amount of prestin protein and reduces its distribution in the outer membrane of hair cells. (13) In addition, the K + channel encoded by KCNQ4, which is responsible for the induction of endolymphatic potential, also decreases significantly under these conditions. (14) Together, these factors affect the micromechanical growth of the cochlea They disrupt both inactive and active cochlear mechanisms (15). So, CH causes a heterogeneity of alterations in the auditory structures. Therefore, various audiological findings are possible. However, audiometric disorders are often characterized by the following features: sensorineural, bilateral, symmetrical, usually high-frequency, variable degrees, often mild, moderate in severity. (16).

2. PATIENTS and METHODS

This cross-sectional study was conducted in patients diagnosed to have primary CH & being followed up in Pediatric Endocrinology Clinic in Children Welfare Teaching Hospital – Medical city / Baghdad. The diagnosis of CH was based on low serum total T4\ f T4 & elevated serum thyroid stimulating hormone level(TSH) according to reference ranges(2). Thyroid ultrasonography performed routinely in our hospital for all patients at time of initial evaluation of CH, however one patient presented with CH & thyroglossal duct cyst underwent thyroid radio-active iodine scanning.

A total of eighty patients were seen, only sixty seven patients with primary hypothyroidism between the ages of one week to 16 years were included in the study (13 patients were excluded from the study because of history of familial hearing loss , past history of significant neurological insult like bacterial meningitis or head trauma , history of recurrent otitis media or any other ear disease , significant neonatal problems such as very low birth weight , hyperbilirubinemia , mechanical ventilation & use of ototoxic drugs & those with incomplete investigations). Patients with central hypothyroidism & autoimmune thyroid disease were excluded from the start.

The clinical & biochemical data are conducted into a prestructured forma taken by reviewing the medical records of fifty five (55) patients who previously diagnosed with CH, whereas the twelve patients who are newly diagnosed, complete physical examination & laboratory investigations performed for them. The forma consist information regarding age, sex, age at diagnosis of CH, initial & last thyroid function test, bone age at the time of diagnosis & at the time of the study. Hearing acuity was assessed in all (67) patients with CH. A detailed audiological examination was carried by the same audiologist in the hearing assessment & audiography clinic of Baghdad Teaching Hospital-Medical city & on same instruments. Otoscopy was performed for all children to ensure that there was no wax or perforation. Those with otitis media, hearing acuity was assessed after the otitis media had been treated medically & cured. The choice of hearing assessment tool was based on the patient`s age & the ability to cooperate & included the following:

Otoacoustic emissions (OAEs) are cochlear sounds that can be recorded through a microphone in the ear canal. They are the result of the movement of sensory hair cells in the cochlea when they energetically respond to auditory stimulation. OAEs provides a simple, effective, non-invasive objective indicator of healthy cochlear function. OAE screening is widely used in general newborn hearing screening programs (17).

The Auditory Brain Response (ABR) is an objective test that assesses the integrity of the auditory system, from the cochlear level to the lower part of the brain. An ABR test is often ordered if a newborn fails a screening test (OAE) or, for older children, if there is a suspicion of hearing loss that has not been confirmed by more routine hearing tests (18).

Pure tone audiometry (PTA) is the key hearing test used to determine hearing sensitivity & hearing loss in response to pure tone stimuli of different frequencies within the normal range of human speech (normal hearing in the frequency range of ≤ 25 dB). PTA is a subjective & behavioral measurement of a hearing threshold, thus it is only used in adults & children old enough to cooperate with test procedure.(19)

Free field examination & OAE was performed for children aged 3 years or below, after two tests without OAE signals, they were referred for ABR test. Subjects with both OAE & ABR abnormal test results were considered to have hearing problem , whereas children above 3years , free field & PTA used to evaluate hearing acuity.

3. RESULTS

The study population consisted of (67) patients with primary CH. The majority of children were in the age group of 1-5 years with female to male ratio of 1.09:1. Eleven patients (16.4%) out of (67) child with CH are diagnosed in the first two weeks of life.(Table 1 & Figure1). Only 5 (7.5%) out of 67 patients with CH have hearing loss.(Figure 2). One (3.8%) patient out of (26) child at or below 3 years of age had hearing loss & the other 4 (9.7%) out of (41) child were above 3 years.(Table 2). Five cases with CH had hearing loss, only one case present with profound hearing loss in both ears, 2 cases present with severe hearing loss in one ear, 3 cases present with moderate hearing loss, 2 of them in one ear & the other in both ears.(Table 3). Five patients with HL, 4 of them were females. Three patients were below one year at time of diagnosis of CH, the older 2 patients had delayed bone age at presentation. The patients with HL had very high TSH level at diagnosis. Thyroid ultrasound showed normal size thyroid gland in 2 patients, 2 patients with absent thyroid & one with thyroid enlargement. Only one patient had average bone age at time of the study. Last TSH level was normal in 3 patients & elevated in 2 of them. Severity of HL were in the range of moderate, severe & profound with 3 patients had bilateral & 2 with unilateral HL. (Table 4)

Table 1. Age and sex distribution of the studied group

Variable		No. of patients	%
Age (year)	< 1 year	16	23.8
	1-5 years	25	37.3
	5-10 years	18	26.8
	> 10 years	8	11.9
Sex	Female	35	52.3
	Male	32	47.7
Total		67	100.0%

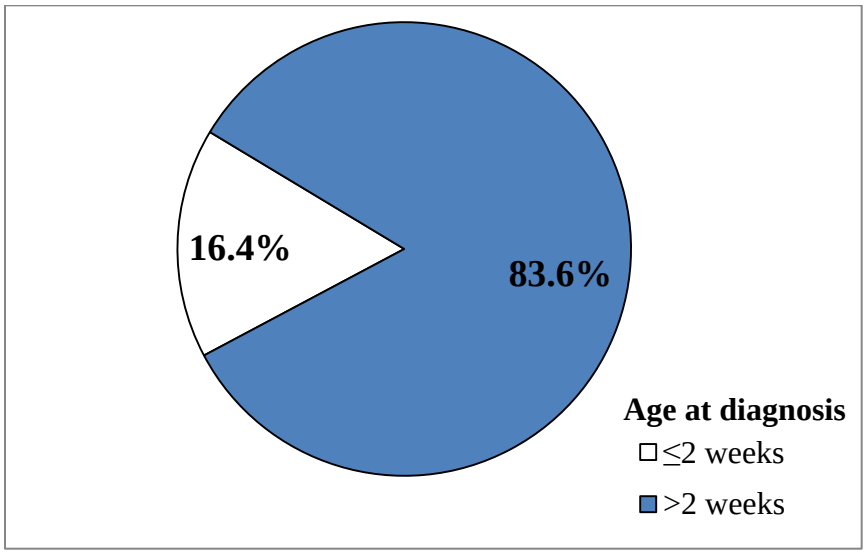

Figure 1. Distribution of patients according to age at diagnosis

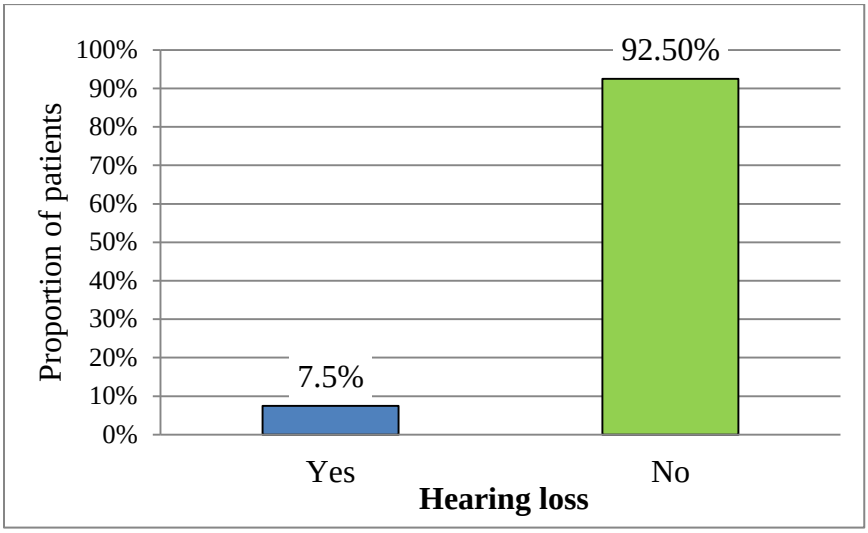

Figure 2. Distribution of hearing loss status among the studied group

Table 2. Association between hearing loss status and age of the patients

Age (year)	Hearing loss				Total	
	Yes		No			
	No.	%	No.	%	No.	%
≤3 years	1	3.8	25	96.2	26	100.0
>3 years	4	9.8	37	90.2	41	100.0
Total	5	7.5	62	92.5	67	100.0
P. value = 0.400						

Table 3. Hearing level characteristics of each ear of patients with hypothyroidism

Ears with hearing loss >25 dB	Case 1	Case 2	Case 3	Case 4	Case 5	Total
Mild 26-40 dB	-	-	-	-	-	0
Moderate 41-70 dB	-	RT	RT&LT	LT	-	3
Severe 71-90 dB	-	LT	-	-	RT	2
Profound >90 dB	RT&LT	-	-	-	-	1
RT; right, LT; left						

Table 4. *Characteristics of patients with congenital hypothyroidism and sensorineural hearing loss*

Case	Sex	Age at diagnosis of CH	Bone age at diagnosis of CH in years	TSH level at diagnosis of CH uIU/ml	Thyroid U/S	Bone age at time of the study in years	TSH level at time of the study uIU/ml	Age at diagnosis of HL in years	Severity of Sensorineural HL
1	F	6 month	-	75	Absent thyroid	8	2.1	8.5	Bilateral. moderate
2	F	11 month	-	62	Absent thyroid	8.2	70	10.4	RT-moderate LT-severe
3	F	4 month	-	100	Normal size	1	0.8	2.8	Unilateral. moderate
4	F	10 year	7.5	36.6	Enlarged thyroid	9.2	21.6	12	Unilateral. severe
5	M	8 year	4.2	75	Normal size	fused	2.3	15.5	Bilateral. profound

4. DISCUSSION

Hearing loss (HL) is not rare in patients with CH & it is worth to remember that articulatory speech defect is fairly common in CH, so it is justified to wonder whether some patients have an undiagnosed hearing loss. The prevalence of HL in this study was five patients (7.5%) (one of them aged below 3 yr. & the other four were above 3 yr.) & this is similar to (7.7%) found in Dayal D et al study (20) which is carried on (77) child between 6 months & 12 years, but higher than (3.2%) in Hashemipour M et al study (21) & involved (94) child with CH below 3 years of age. The prevalence of (7.5%) is much lower than (35%) in P Prentice et al study (22) which included (102) neonates with CH. This difference in the results can partly be attributed to sample size compared to Hashemipour & P Prentice studies, difference in the age at hearing screening test & methods of hearing assessment as in Hashemipour & P Prentice studies which used only OAE & ABR for hearing screen or differences in the ethnicity & genetic factors in different patient populations. There are different reports about hearing impairment & time of starting treatment. Although in this study, the prevalence of children diagnosed within first two weeks of life was (16.4%) & all underwent audiologic screen within first thirty months is too small to draw any firm conclusion, but none of them were found to have a HL & this disagree with Hashemipour M et al study (21)in which HL was found in(3.2%) of patients diagnosed primarily during CH screening program & underwent hearing screen within first 3years of life or Bruno R study(23)which demonstrate (25%) of patients diagnosed in the neonatal period have evidence of HL by median age of(15.4)years, whereas all five(7.5%) patients with HL in the present study diagnosed with CH months or years after presentation . This discrepancy between age of starting treatment & risk of HL may be closely related to the etiology & severity of CH or inadequacy of therapy during childhood rather than to the age at diagnosis. Sensorineural deafness was the only type of HL found in subjects of this study (7.5%) & this is similar to (6.45%) in Saffari F et al study (4), but different from P Prentice et al study (24) which identified (35%) with HL, half of them had conductive HL or (9.5%) in Lchtenberger-Geslin et al study (25) who showed (20%) of them had conductive HL & the remainder present with sensorineural HL. This high frequency of sensorineural HL in CH patients suggests that the cochlea is the main structure affected. It has been shown that the complex

process of cochlear differentiation is regulated by the amount of T3 which is locally controlled by type 2 & 3 deiodinases & by thyroid hormone transporters.(26) However, middle ear defects (immature ossicles or otitis) might account for the occurrence of conductive or mixed HL.(27) The severity of HL in the five patients of this study was in the frequency range of moderate, severe & profound. This is largely differ from P Prentice et al study (24) were no patient had severe or profound HL. All the patients presented with mild to moderate HL diagnosed by audiologic screen performed in the neonatal period. This may suggest that hearing impairment is currently undetectable in neonates with screening methods available & some of HL observed in these patients is probably mild congenital progressive HL that does not become severe enough for detection until early childhood when it became more serious & thus detectable.(25) Or severity of HL may be attributed to the type of CH as patients with thyroid a thyrosis & dyshormonogenesis being more frequently affected than those with an ectopic thyroid gland(2 of our patients have thyroid agenesis & 3 have dyshormonogenesis) & this reason was clearly reliable in Bruno R et al study (23) & Lchtenberger-Geslin et al study (25) were the poorest hearing scores recorded in the individuals with athyreosis & gland in situ, whereas Saffari F et al study(4) showed no such association. Another cause for severity of HL in patients of this study may be its association with severity of the disease at time of diagnosis as assessed by extremely elevated TSH level or significant delay of bone maturation or inadequacy of disease control during childhood & this disagree with Lchtenberger-Geslin et al study(25) & Hashemipour M et al study (21) which stated that hearing impairment was not associated with gender, age at levothyroxin treatment initiation or the adequacy of long-term hypothyroidism control during childhood. However, these data should be cautiously interpreted in this relatively small study

5. CONCLUSIONS

Hearing impairment was present in a proportion of patients with CH & its relation to the age of CH diagnosis or disease control during childhood & whether its fixed or progress with time require further study. Early and regular evaluation of hearing acuity and careful followup is required for all children with congenital hypothyroidism.

Ethical Clearance : Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 of ethical principles for medical research involving human subjects. Data and privacy of patients were kept confidentially.

Conflict of interest: Authors declared none

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