

Language disorders in children with congenital hypothyroidism

Haitham M. Mohamed^a, Efat Zaki^a, Adel Abdel Baki Abdall^b,
Mohammed A. Gomaa^b, Marwa M. Abdel Wahab^a

^aDepartments of Phoniatic,

^bOtorhinolaryngology, Faculty of Medicine,
Minia University, Minia, Egypt

Correspondence to Mohammed A. Gomaa,
MD, ENT Department, Minia University
Hospital, Minia 61111, Egypt.
Tel: +20 122 733 9776;
e-mail: magomaa67@gmail.com

Received 20 August 2015

Accepted 4 September 2015

The Egyptian Journal of Otolaryngology
2017, 33:685–690

Introduction

Congenital hypothyroidism (CH) represents one of the most common preventable causes of mental retardation. If fetal hypothyroidism develops, untoward effects may be shown in certain organ systems, including the central nervous system. CH may be associated with hearing and language impairment. It is possible that this impairment may worsen with delay of therapy. Problems in language, auditory processing, and reading may persist in hypothyroid children, particularly if their treatment with l-thyroxin is delayed into the third week of life.

The aim of this study is to estimate the extent of language disorder and detect the factors influencing language acquisition in children with CH.

Patients and methods

This study included 60 children. The study group included 40 children who complained of CH. The age range of this group was 3–8 years. The children of the study group were divided according to the level of thyroid stimulating hormone (TSH) and T4 into two subgroups. The G1 subgroup included children with controlled CH and subgroup G2 included children with uncontrolled hypothyroidism. The results of the study group were compared with those of another group (control group), which included 20 children; both groups were matched for age and sex. The children of both groups were subjected to the protocol of language assessment.

Results and conclusion

The current study showed that the children with uncontrolled CH show delayed language, mental, social age, and intelligence quotient in comparison with children with controlled hypothyroidism and normal children.

There is a need for the diagnosis and treatment of children with CH as soon as possible after birth, preferably no later than the second week of life. It is also important to screen hypothyroid children for hearing problems and to provide remediation in language and reading.

Keywords:

hypothyroidism, language development

Egypt J Otolaryngol 33:685–690

© 2017 The Egyptian Journal of Otolaryngology

1012-5574

Introduction

Hypothyroidism results from the deficient production of thyroid hormone or defect of thyroid hormone receptor activity. Most cases of congenital hypothyroidism (CH) are not hereditary and result from thyroid dysgenesis. Some cases may be familial, usually caused by one of the inborn errors of thyroid hormone synthesis [1].

Children born with CH who lack thyroid hormone during early period of development are at risk of brain damage and mental retardation [2].

The prevalence of CH reported on the basis of nationwide programs for neonatal screening is 1/4000 infants worldwide. The prevalence is lower in Black Americans (1/32 000) and higher in Hispanics and Native Americans (1/2000). The female to male ratio

is 2:1 [1]. Also, Fuggle *et al.* [3] reported that CH may be associated with hearing and language impairment. It is possible that this impairment may worsen with delay of therapy. The problems in receptive language, auditory processing, and reading may persist in hypothyroid children, particularly if their treatment with l-thyroxin is delayed into the third week of life [3].

On psychometric tests, the hypothyroid group was observed to perform significantly lower than nonimpaired hypothyroid at 3 years of age, but seemed to catch up by age 5 and did not differ on

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work noncommercially, as long as the author is credited and the new creations are licensed under the identical terms.

an expressive language test administered at the age of 7 years [4], whereas Rovet and Ehrlich [5] reported that early identification and treatment of CH with newborn screening is associated with almost complete elimination of mental retardation and significantly improved intellectual functioning; however, intelligence quotients (IQs) are significantly and persistently reduced, and subtle impairments may occur in language memory and attention.

The aim of this study is to estimate the extent of language disorder and detect the factors influencing language acquisition in children with CH.

Patients and methods

The current study was approved by the Research Ethics Committee of the Faculty of Medicine, Minia University. Informed consent was signed by the parents/guardian of the studied children. The study was carried out at the Departments of Otorhinolaryngology and Phoniatics at Minia University Hospital in the period 2012–2013.

The study group included 40 children. There were 13 (32.5%) males and 27 (67.5%) females (mean age: 68.8 ±18.6 months, range: 30–96 months).

The children of the study group were divided according to the level of thyroid stimulating hormone (TSH) and T4 into two groups. G1 subgroup included children with controlled CH and subgroup G2 included children with uncontrolled hypothyroidism. In G1, there were eight (36.4%) males and 14 (63.6%) females (mean age: 70.2±18.036 months, range: 30–90 months). In G2, there were five (27.8%) males and 13 (72.2%) females (mean age: 67.2 ±19.86 months, range: 41–96 months).

The control group G3 included 20 children. There were 11 (55%) males and nine (45%) females (mean age: 70.8±14.5 months, range: 43–90 months). The children of this group had normal levels of TSH and T4.

The patient and control groups were subjected to the following:

- (1) Full assessment of personal and medical history from parents that included natal and perinatal history.
- (2) Ear, nose, and throat examination of the children.
- (3) General medical examination.
- (4) Audiological evaluation:

Audiological evaluation was carried out to ensure normal hearing sensitivity (tympanogram, pure tone audiometry, auditory brain stem evoked response to identify hearing sensitivity).

- (5) Laboratory evaluation:

Blood samples were obtained for assay of T3, T4, and TSH.
- (6) Language assessment:
 - (a) Evaluation of various aptitudes by formal testing:
 - (i) Cognitive age (mental age): using the Stanford Binet Intelligence Scale [6] or the nonverbal intelligence test of Snijders-Ommen [7].
 - (ii) Social age: using the Vineland Social Maturity Scale [8].
 - (b) Language evaluation:

The Arabic Language Test was used [9]. The language test items include attention of the child by observation, receptive part of the semantics, expressive part of the semantics, receptive part of the syntax, the expressive part of syntax, pragmatics, and prosody [9].

Statistical analysis

Data were collected and analyzed using SPSS software (version 19 for Windows; SPSS Inc., Chicago, Illinois, USA). An independent-sample *T*-test was used to compare quantitative data and the χ^2 -test was used to compare qualitative data.

Results

The current study was carried out on 60 children; the study group included 40 children. There were 13 (32.5%) males and 27 (67.5%) females.

The children of the study group were divided according to the level of TSH and T4 into two groups. G1 subgroup included children with controlled CH and subgroup G2 included children with uncontrolled hypothyroidism. The control group G3 included 20 health children with normal TSH and T4. Table 1 shows the sociodemographic data of the groups.

Intelligence quotient, mental, social age, and language assessments

Our study showed that the mean IQ of the children in G1 was 78.7±10.9 (range: 51–92), the mean IQ of the children in G2 was 56.3±5.6 (range: 50–66), and the mean IQ of the children in G3 was 81.5±17.5 (range: 48–99).

The mean mental age of the children in G1 was 61.9±17.1 (range: 25–85), the mean mental age of the children in G2

Table 1 Comparison between the three groups in demographic data

Data	G1 (N=22)	G2 (N=18)	G3 (N=20)	P_1	P_2	P_3
Age				0.9	0.5	0.5
Range	30–90	41–96	43–90			
Mean±SD	70.2±18.03	67.2±19.8	70.8±14.5			
Sex [n (%)]				0.3	0.1	0.8
Male	8 (36.4)	5 (27.8)	11 (55)			
Female	14 (63.6)	13 (72.2)	9 (45)			

Table 2 Comparison between three groups in the intelligence quotient test, and mental, social, and language age

Data	G1 (N=22)	G2 (N=18)	G3 (N=20)	P_1	P_2	P_3
IQ test				0.01*	0.001**	0.001**
Range	51–92	50–66	48–99			
Mean±SD	78.7±10.9	56.3±5.6	81.5±17.5			
Mental				0.01*	0.001**	0.002**
Range	25–85	22–80	25–93			
Mean±SD	61.9±17.1	42.6±18.6	74.3±18.7			
Social				0.02*	0.001**	0.003**
Range	2–80	19–77	20–91			
Mean±SD	57.3±19.9	37.8±20.1	69.9±19.6			
Language				0.02*	0.001**	0.001**
Range	25–90	2–40	24–84			
Mean±SD	42.4±18.3	22.8±12.6	56±20.3			

IQ, intelligence quotient. *,** Level of significance when $P<0.05$.

was 42.6 ± 18.6 (range: 22–80), and the mean mental age of the children in G3 was 74.3 ± 18.7 (range: 25–93).

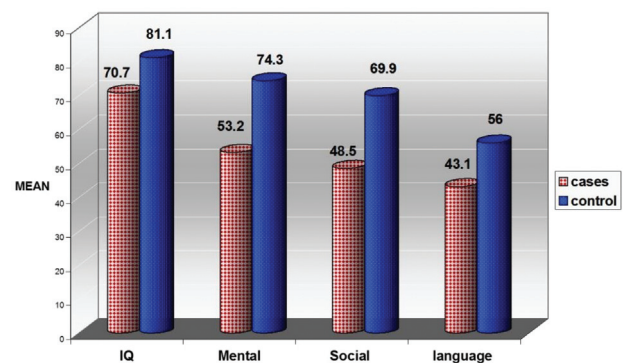
The social age of the children in G1 was 57.3 ± 19.9 (range: 2–80), the social age of the children in G2 was 37.8 ± 20.1 (range: 19–77), the social age of the children in G3 was 69.9 ± 19.6 (range: 20–91).

The mean language age of the children in G1 was 42.4 ± 18.3 (range: 25–90), the mean language age of the children in G2 was 22.8 ± 12.6 (range: 2–40), and the mean language age of the children in G3 was 56 ± 20.3 (range: 24–84).

The previous data indicate statistically significant differences between the study and the control group in the IQ and language age ($P<0.05$), highly statistically significant differences between the study and the control group in the mental and social age ($P<0.01$), and highly statistically significant differences between G1 and G2 in the IQ, mental, social, and language age ($P<0.01$). Table 2 shows a comparison between the three groups in IQ test, mental, social, and language age. Figure 1 shows a comparison between the study and the control groups in the IQ test, mental, social, and language age.

Level of TSH and T4 assessment

The mean level of TSH in children in G1 was 1.6 ± 0.2 (range: 1.4–3.3), that of children in G2 was 14.3 ± 4.6

Figure 1

Comparison between study and control as regarding IQ test, mental, social and language age.

(range: 5.5–20.3), and that of children in G3 was 2.6 ± 0.3 (range: 1.9–3.2).

The mean level of T4 in children in G1 was 1.2 ± 0.2 (range: 1.1–2.1), that of children in G2 was 0.6 ± 0.2 (range: 0.3–1.4), and that of the children in G3 was 1.5 ± 0.2 (range: 1.1–2.1). Table 3 shows a comparison between three groups in TSH and T4.

A highly positive significant correlation was found between the language, mental, social age, and IQ with the level of T4 in G1 and G2 ($r=0.76$).

A highly negative significant correlation was found between the language, mental, social age, and IQ

Table 3 Comparison between three groups in TSH and T4

Data	G1 (N=22)	G2 (N=18)	G3 (N=20)	P_1	P_2	P_3
TSH				0.6	0.001**	0.001**
Range	1.4–3.3	5.5–20.3	1.9–3.2			
Mean±SD	1.6±0.2	14.3±4.6	2.6±0.3			
T4				0.005**	0.001**	0.002**
Range	1.1–2.1	0.3–1.4	1.1–2.1			
Mean±SD	1.2±0.2	0.6±0.2	1.5±0.2			

TSH, thyroid stimulating hormone. **Level of significance when $P < 0.05$.

Table 4 Correlation between language, mental, social, intelligence quotient, and the levels of TSH and T4

	TSH			T4		
	Correlation	Significance	r	Correlation	Significance	r
Language age	–	HS	0.91	+	HS	0.90
Mental age	–	HS	0.82	+	HS	0.88
Social age	–	HS	0.76	+	HS	0.83
IQ	+	HS	0.66	+	HS	0.91

HS, highly significant; IQ, intelligence quotient; TSH, thyroid stimulating hormone.

Table 5 Comparison between study and control groups in tympanometry and audiometry

Data	Cases (N=40) [n (%)]	Control (N=20) [n (%)]	P
Tympanometry			0.1
Type A	33 (82.5)	20 (100)	
Type B	3 (7.5)		
Type C	4 (10)		
Audiometry normal	40 (100)	20 (100)	0.5

with the level of TSH in G1 and G2 ($r = -0.87$). Table 4 shows the correlation between language, mental, social, IQ, and the level of TSH and T4.

The audiological assessment

There was no statistical difference between the study and control groups in the audiological evaluation ($P > 0.05$). Table 5 shows a comparison between study and control groups in tympanometry and audiometry.

Discussion

CH represents one of the most common preventable causes of mental retardation. If fetal hypothyroidism develops, unwanted effects may be found in certain organ systems, including the central nervous system and skeleton. However, most infants with CH appear normal at birth [10]. Thyroxin is a major regulator of the mammalian brain development; an important role for thyroxin can be expected from early fetal life until the completion of central nervous system growth, several years beyond birth. Lack of thyroxin, during the critical period of central nervous system responsiveness to this hormone, results in delay of myelination and dendritic arbor [11].

The current study aimed to investigate the language developmental outcomes of the children with CH (study group) in comparison with children with normal thyroid functions (control group); there was a statistically significant difference between the children with hypothyroid function and children with normal thyroid function in IQ, mental, and social age. Moreover, there was a highly statistically significant difference between the children with controlled hypothyroidism and those with noncontrolled hypothyroidism in the IQ, social, and mental age. Miller *et al.* [12] reported that the treated hypothyroid group had significantly increased verbal memory retrieval. Results suggest that specific memory retrieval deficits associated with hypothyroidism can resolve after replacement therapy with l-thyroxine.

Koibuchi and Chin [13] studied children with severe CH, treated at a mean age of 5 weeks with 1 g/kg/day of l-thyroxine; they had mean IQ scores 10–22 points below that of their siblings from 18 months until 12 years of age (the last time point studied), whereas those with moderate CH had IQ scores similar to those of control children.

Hrytsiuk *et al.* [14] carried out neurological and psychological assessments on 30 patients aged 2.7–21 years (mean: 9.4 years) who were being treated for hypothyroidism starting before the age of 2 years. Their IQ scores were within the normal range (71–122; mean: 92.4), but 77% showed at least one sign of impaired brain function. Clumsiness was found in 33%, behavior disorders in 23%, language disorders in 20%, learning disorders in 26%, squint in 53%, nystagmus in 10%, and minor motor disorders in

50% [14]. The current study is in agreement with that of Miller *et al.* [12], Koibuchi and Chin [13], and Hrytsiuk *et al.* [14], who showed affection of IQ, language development, and mental age in CH.

MRI showed that signal intensities from various white matter areas were comparable in untreated patients and control participants. There was also no change in signal intensities after thyroxine replacement. MRI was shown to have identify a delay in myelination in patients with untreated CH; an improvement was documented after thyroxine replacement [15].

The current results obtained from the Arabic language test indicated a significant difference between children with hypothyroidism and children with normal thyroid function in the language age. Moreover, there was a highly statistically significant difference between the children with controlled hypothyroidism and those with noncontrolled hypothyroidism in language age. These results are in agreement with those of Glorieux *et al.* [16], who studied the mental development of hypothyroid infants at the age of 12, 18, and 36 months and found that there was no difference between the global quotient in the 12 months. However, at 18 months and 36 months of age, the hypothyroid group had a significantly lower mean global quotient than the control group. They stated that their results may represent the manifestations of brain damage that occur even with early detection and treatment of hypothyroidism [16].

Fuggle *et al.* [3], Rovet *et al.* [1] and Rovet and Ehrlich [5] found significantly improved intellectual functioning; however, significantly and persistently reduced intellectual quotients with subtle impairments may occur in language memory and attention in hypothyroid children. Miller *et al.* [12] reported in their study that the treated hypothyroid group had significantly increased verbal memory retrieval. Results suggest that specific memory retrieval deficits associated with hypothyroidism can resolve after replacement therapy with l-thyroxine [12]. Our results are not in agreement with those of Denman [17], who found that the CH group did not differ from control children on tests of phonological processing (WJRMT Word Attack), writing (test of written language; TOWL), or spelling (WRATR spelling). The results of the supplementary tests also indicated no differences in language and memory tasks [17].

Komur *et al.* [18] reported that cognitive, language, and global motor scores in addition to receptive communication, expressive communication, fine

motor, and gross motor subscores in children with CH were statistically significantly lower than those in the control group, and their study concluded that despite early and effective treatment in newborns with CH, retardation in neurological developmental was detected. This could be related to influences on neurodevelopment in the intrauterine period. Current data are in agreement with our results as uncontrolled hypothyroidism score lower than controlled hypothyroid children as well as normal ones regarding language development [18]. Also, our results in agreement with those of Gejão and Lamônica [19], who reported that most of the children in their study showed adequate performance in the skills evaluated, whereas for children with altered performance, larger deficits were observed in the language section, in the expressive aspects, and in the cognitive section.

Bargagna *et al.* [20] reported in their study that the mean total scores of the study group in cognitive tests were within the normal range; instead, motor and language impairments were noted. These skills are significantly correlated with pretreatment serum thyroxine. This study supports our results as language impairment is very crucial in hypothyroid children, and screening and early detection of hypothyroid babies is essential [20].

The current study concludes that there is a need for the diagnosis and treatment of children with CH as soon as possible after birth, preferably no later than the second week of life. It is also important to screen hypothyroid children for hearing problems and to provide remediation in language and reading.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- 1 Kliegman E, Behrman D, Jenson F. Nelson text book of pediatric. Vol. 5. 17th edn. Noble: Barnes; 2007:122–160.
- 2 Rovet J, Daneman D. Congenital hypothyroidism: a review of the current diagnostic and treatment practices in relation to neuropsychologic outcome. *Paediatr Drugs* 2003; 5:141–149.
- 3 Fuggle PW, Grant DP, Smith I. Intelligence, motor skills and behavior at 5 years in early treated congenital hypothyroidism. *J Pediatr* 1988; 15:570–574.
- 4 Rovet J, Ehrlich R, Sorbara D. Intellectual outcome in children with fetal hypothyroidism. *J Pediatr* 1987; 110:700–704.
- 5 Rovet JF, Ehrlich RM. Long-term effects of L-thyroxine therapy for congenital hypothyroidism. *J Pediatr* 1995; 126:380–386.
- 6 Terman LM, Merrill MA. Stanford Binet intelligence scale. Boston: Houghton Mifflin Company; 1972; 8:100–203.

- 7 Snijders-Ommen JA. Nonverbal intelligence test for deaf and hearing subjects. Holland: J.B. Wolters; 1939; 2:55–99.
- 8 Doll EA. Vineland social maturity scale Vol. 2. USA: Minneapolis American Services; 1965. p. 99–200.
- 9 Kotby MN, Khairy A, Baraka M, Rifaie N, El Shobary A. Language testing of Arabic speaking children. Proceeding of the XXIII world congress of International Association of Logopedics and Phoniatrics; Cairo; 5 August 1995; p. 6–10.
- 10 Zakarajia M, Mckenize JM, Eidson MS. Transient neonatal hypothyroidism: characterization of maternal antibodies to the thyrotropin receptor. *J Clin Endocrinol Metab* 1990; 70:1239–1245.
- 11 Bernal J, Nunez J. Thyroid hormones and brain development. *Eur J Endocrinol* 1995; 133:390–398.
- 12 Miller KJ, Parsons TD, Whybrow PC, van Herle K, Rasgon N, van Herle A, *et al.* Memory improvement with treatment of hypothyroidism. *Int J Neurosci* 2006; 116:895–906.
- 13 Koibuchi N, Chin W. Thyroid hormone action and brain development. *Trends Endocrinol Metab* 2000; 11:123–128.
- 14 Hrytsiuk I, Gilbert R, Logan S, Pindoria S, Brook CG. Starting dose of levothyroxine for the treatment of congenital hypothyroidism: a systematic review. *Arch Pediatr Adolesc Med* 2002; 156:485–491.
- 15 Alves C. Changes in brain maturation by magnetic resonance imaging in congenital hypothyroidism. *J Pediatr* 2004; 115:6000–6003.
- 16 Glorieux J, Desjardins M, Letarte J, Morissette J, Dussault JH. Useful parameters to predict the eventual mental outcome of hypothyroid children. *Pediatr Res* 1988; 24:6–8.
- 17 Denman SB. Neuropsychology memory scale. Charleston, SC: Springer; 1984.
- 18 Komur M, Ozen S, Okuyaz C, Makharoblidze K, Erdogan S. Neurodevelopment evaluation in children with congenital hypothyroidism by Bayley-III. *Brain Dev* 2013; 35:392–397.
- 19 Gejão MG, Lamônica DA. Development skills in children with congenital hypothyroidism: focus on communication. *Pro Fono* 2008; 20:25–30.
- 20 Bargagna S, Astrea G, Perelli V, Rafanelli V. Neuropsychiatric outcome in patients with congenital hypothyroidism precariously treated: Risk factors analysis in a group of patients from Tuscany. *Minerva Pediatr* 2006; 58:279–287.