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Growth and Developmental Milestones in Children with Congenital Hypothyroidism Attending Assiut Health Insurance Clinic

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A B S T R A C T

Objective: To determine the effect of Congenital Hypothyroidism (CH) on growth and development of children aged 1–60 months. **Method:** A cross-sectional study including 118 children with CH and 236 normal children was conducted in Assiut, Egypt. Growth was measured by weight and length/height. Developmental delay was screened using Ages and Stages Questionnaire. **Results:** Mean age in both groups was 19.6 months. Mean weight of children with CH was 6991.3±1907.4 gm versus 6912.3±188.2 gm for normal children in children aged 1-<24 months and 14587.2±2344 gm versus 14299.4±1997gm among children aged 24-60 months, respectively. Overweight (7.6% versus 2.2), stunting (47.5% versus 25%) and developmental delays in communication (14.4% versus 2.5%), gross motor (29.7% versus 5.9%), fine motor (13.6% versus 5.9%), problem solving (10.2% versus 3.8%), and personal–social (11.9% versus 1.3%) domains were significantly higher among children with CH compared to normal children. Regarding thyroid function, 15% and 23% of children with CH revealed overt and subclinical hypothyroidism respectively. Overt hypothyroidism showed significantly higher developmental delays than either euthyroid or subclinical cases in the communication gross motor, fine motor, and personal–social domains (64.7%, 42.9%, 43.8% and 42,9% respectively). **Conclusion**: Children with CH were significantly overweight, stunted and developmentally delayed compared to normal children. Impaired thyroid function was not associated with growth defects but overt hypothyroid children showed significant developmental delay. IQ testing and continuous monitoring are essential for all children with CH. Efficiently organized recording systems, treatment documents, and compliance and follow-up assessment results can facilitate hassle-free health-card retrieval.

INTRODUCTION

Congenital hypothyroidism (CH) is defined as a thyroid-hormone deficiency that develops in the perinatal period and is present at birth.[1] CH is among the most prevalent congenital disorders in the Middle Eastern countries including Egypt.[2,3] Before implementation of neonatal screening programs; when CH diagnosis was done on clinical basis, worldwide incidence of CH varied from 1:6,000 to 1:10,000 newborns.[4,5] After neonatal screening, the worldwide incidence of CH raised to be 1:3,000–1:4,000 newborns, with regional variations based on ethnicity and behavioral factors.[6,7]

However, the recent years have witnessed significant worldwide increases in CH incidence,[6] which can be attributed to a reduction in the screening cutoff levels for the thyroid stimulating hormone (TSH) and environmental factors like iodine deficiency.[8]

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Special screening procedures for high-risk neonates together with improvements in neonatal medical care have increased the survival rates of preterm babies.[8] The Egyptian Ministry of Health and Population implemented a neonatal screening program that has a coverage rate above 90% for CH.[9]

The effects of TSH on somatic growth are manifested during pregnancy and extend through the early years of life. Indeed, the first five years of a child's life are the time when the early central nervous system develops, which is highly affected by TSH levels. It is known that the thyroxin (T_4) hormone plays a pivotal role in musculoskeletal and brain growth;[10] moreover, TSH promotes healthy somatic growth. Meanwhile, patients with untreated CH are at risk for severe somatic growth and developmental delays.[3,11,12] Irreversible effects of TSH deficiency include delayed developmental milestones.[12.] Undiagnosed or untreated CH causes irreversible mental disability,[13] culminating in personal suffering and heavy social and economic responsibilities for families and the country. Fortunately, CH treatment is simple, inexpensive, and effective.[14] The longer CH is untreated or uncontrolled, the greater the risk of low IQ, obesity, and short stature.[12,15] This study aims to assess the growth and development among children with CH in the critical age group (1-60 months).

METHOD

An analytic cross-sectional study was conducted in Sidi-Galal health insurance clinic, Assiut city, Assiut Governorate, Egypt. All infants who test positive for CH on neonatal screening are referred to Sidi-Galal clinic for treatment and follow-up every Saturday and Wednesday. Therefore, this clinic was used to recruit patients with CH up to 60 months. Normal children in the comparison group were recruited from three primary health care centers (PHCs), one urban and two rural, in Assiut Governorate.

Sample size was calculated using Open-source Epi info software stat calc function for cross sectional study at 95% confidence interval and 80% power of the test. Based on a study in Fayoum[16], Egypt, 38.9% of children with CH showed stunting and the finding in Egypt Demographic and Health Survey (EDHS),[17] 2014 that 21.4% of children under 5 showed stunting. Based on comparative group/ cases ration equal 2, the required sample was 87 children with CH and 173 normal children.

The sample size was increased to overcome any potential difficulties in retrieving children's data, so all mothers or caregivers of children aged 1–60 months who had been diagnosed with CH and who attended Sidi-Galal clinic during the year 2018 (118 cases) were interviewed. The comparison group recruited was 236 children. The inclusion criteria were as follows: (1) Children with CH: children were aged 1–60 months, CH had been detected on Egypt's neonatal screening test and confirmed by diagnostic test. Children had been treated with levothyroxine and followed up at Sedi Galal clinic. There were free of any other congenital or chronic disease. (2) Comparison group: healthy children, free from any congenital or chronic disease, and attending one of the PHCs for any health services (vaccination, healthy baby clinic, outpatient treatment for acute conditions). They were matched to cases in age group to apply developmental screening using the Ages and Stages Questionnaire third edition (ASQ3) for each age group. They mere matched to cases by gender to overcome the traditional differences in nutritional status between boys and girls, especially in rural areas where boys receive most of families 'concern.

Data on age, sex, and residence for every child was obtained and the latest thyroid function test results for the children with CH were retrieved from their records by the researcher.

Clinics' nurses measured the children's weight and height/length using calibrated instruments under direct supervision of the researcher. Children under 24 months were weighed with an infant scale, and older children were weighed with the adult scale. Length of infants under 24 months was measured in recumbent position using an infantometer, and the heights of children aged 24–60 months were measured in supine position using a stadiometer. Growth status was classified according to the WHO growth charts included on the Egyptian child growth monitoring cards and vaccinations for boys and girls.[18] Specifically, weight for age was classified as follows: Low = below 15^{th} percentile; normal = between 15^{th} and 85^{th} percentile; and overweight = above 85th percentile. Regarding length/height for age, stunted and normal growth rates were classified as below 15^{th} percentile and above 15^{th} percentile respectively.

Children were also screened for their developmental milestones using the ASQ3, which is a validated tool available in many languages including Arabic (86% sensitivity, 85% specificity, 86% validity).[20] The

Table (1): Sociodemographic characteristics of congenital hypothyroidism cases and normal children, Assiut Governorate

Variable	CH (*N* = 118) *N* (%)	Normal (*N* = 236) *N* (%)	S. test	P value
Gender:				
Female	62 (52.5)	124 (52.5)	X^2=0	1.00
Male	56 (47.5)	112 (47.5)		
Age:				
<24 m	75 (63.6)	150 (63.6)	X^2=0	1.00
24–60 m	43 (36.4)	86 (36.4)		
Residence:				
Rural	75 (63.6)	126 (53.4)	X^2=3.3	0.007
Urban	43 (36.4)	110 (46.6)		
Weight:	Mean ± SD (in grams)			
<24 m	6991±1907	6912±188	t=0.3	0.4
24–60 m	14587±2344	14299.4±1997	t=0.7	0.08

scale measures development in children in 21 age groups across five domains: communication, gross motor, fine motor, problem solving, and personal–social. Each domain comprises six questions, for a total of 30, with closed answers scored by converting each provided answer to a numeric value: 10 = most of the time, 5 = sometimes, and 0 = not yet.[19] The total score of each domain was summed and compared to the predetermined cutoff provided in the score guidance that classifies children as having normal or delayed development.[20] For the thyroid function tests of children with CH, thyroid function was All data management processes; data entry, cleaning, revision, and recoding (if required) was done using SPSS version 20 for Windows (SPSS Inc., Chicago, IL, USA).

Descriptive statistics: mean $\pm$ SD for quantitative variables, frequency, and percent for qualitative variables. Inferential statistics; chi-square/ Fisher's exact test was used to test significance between qualitative variables, and odds ratio was estimated. Student *t*-test/ANOVA test were used to compare means between two or more groups of continuous variables. $P < 0.05$ was set as the significance level for all tests.

Ethical committee of faculty of medicine, Assiut University approved the study protocol. Administrative approvals were obtained from the Ministry of Health and the health insurance sector of Assiut Governorate. Informed oral consent was obtained from the children's caregivers. They were assured about confidentiality of data. A clinic consultant closely monitored all children with overt hypothyroid, growth impairment, and developmental delay, with adjustments of the L-thyroxin dose to reach euthyroid state and complete catch-up. categorized as follows:[21,22] Overt hypothyroidism: TSH above 9 µU/ml and FT4 below 10.3 pmol/L; Subclinical hypothyroidism: TSH above 9 µU/ml and FT4 range 10.3-28.3 pmol/L; Euthyroid: TSH 0.8 to 9 µU/ml and FT4 10.3 to 28.3 pmol/L.

A pretest study was conducted on 30 children (10 with CH and 20 healthy children) to test the feasibility of administering the interview questionnaire and if it requires any modifications. No modifications were required. From the pretest children, children with CH only were included in the study.

RESULTS

More than half of the children with CH (52.5%) were girls and about two thirds of children with CH were below 24 months of age and residents of rural areas (Table 1).

Table (2): Growth in children with congenital hypothyroidism and normal children, Assiut Governorate

Variable	CH (*N* = 118) *N* (%)	Normal (*N* = 236) *N* (%)	X^2	*P*	OR (CI)
Weight for age					
15th–85th percentile	92 (78.0)	183 (77.5)			Ref
Below 15th percentile	17(14.4)	48 (20.3)	1.3	0.30	
Above 85th percentile	9 (7.0)	5 (2.2)	5.6	**0.02**	3.4 (1.2–9.7)
Length/height for age					
Above 15th percentile	62 (52.5)	177 (75.0)	18.1	**< 0.001**	1.9 (1.4–2.5)
Below 15th percentile	56 (47.5)	59 (25.0)			

As regards weight for age, there were significantly more overweight children among the CH group compared to the comparison group (7.6% versus 2.1% respectively). Regarding length/height for age,

Table (3): Developmental milestones among children with congenital hypothyroidism and normal children, Assiut Governorate

ASQ3 Domain	CH (118) *N* (%)	Normal (236) *N* (%)	X^2	*P*	OR (CI)
Communication					
Normal	101 (85.6)	230 (97.5)	18.2	**<0.001**	5.6 (2.3–3.9)
delayed	17 (14.4)	6 (2.5)			
Gross motor					
Normal	83 (70.3)	222 (94.1)	37.1	**< 0.001**	5 (2.8–9.8)
delayed	35 (29.7)	14 (5.9)			
Fine motor					
Normal	102 86.4)	222 (94.1)	5.9	**0.02**	2.3 (1.2–4.5)
delayed	16 (13.6)	14 (5.9)			
Problem solving					
Normal	106 89.8)	227 (96.2)	5.7	**0.02**	2.6 (1.2–6.1)
delayed	12 (10.2)	9 (3.8)			
Personal–social					
Normal	104 (88.1)	233 (98.7)	19.3	**<0.001**	9.3 (2.7–1.8)
delayed	14 (11.9)	3 (1.3)			

Table (4): Growth in children with congenital hypothyroidism according to sociodemographic characteristics, Assiut Governorate

Growth Parameters	Age Group		Gender		Residence	
	1–<24 m (*N* = 75)	**24–60 (*N* = 43)**	**male (*N* = 56)**	**female (*N* = 62)**	**Rural (*N* = 75)**	**Urban (*N* = 43)**
weight for age (*N* = 118)						
15th–85th percentile *N* = 92	57 (76.0%)	35 (81.3%)	40 (71.0%)	52 (83.9%)	59 78.7%)	33 76.7%)
Below 15th percentile *N* = 17	11 (14.7%)	6 (14.0%)	11 (19.6%)	6 (9.7%)	10 (13.3%)	7 (16.3%)
Above 85th percentile *N* = 9	7 (9.3%)	2 (4.7%)	5 (8.9%)	4 (6.5%)	6 (8.0%)	3 (7.0%)
	X^2 = 0.9	*P* = 0.6	**X^2 = 2.8** *P* = 0.2		**X^2 = 0.2**	*P* = 0.9
length /height for age (*N* = 118)						
Above 15th percentile *N* = 62	37 (49.3%)	25 (58.1%)	28 (50.0%)	34 (54.8%)	44 (58.7%)	18 (41.9%)
Below 15th percentile *N* = 56	38 (50.7%)	18(41.9%)	28 (50.0%)	28 (45.2%)	31 (41.3%)	25 (58.1%)
	X^2 = 0.9	*P* = 0.4	**X^2 = 0.3**	*P* = 0.6	**X^2 = 3.1**	*P* = 0.08

stunting was significantly higher among children with CH compared to normal children (47.5% versus 25.0% respectively). (Table 2).

Significantly higher developmental delays were reported among children with CH than normal children across all the five ASQ3 domains: communication (14.4% versus 2.5%); gross motor (29.7% versus 5.9%); fine motor (13.6% versus 5.9%); problem solving (10.2% versus 3.8%); and personal–social (11.9% versus 1.3%) respectively (Table 3).

Although the difference was statistically insignificant, both overweight and stunting were higher among children below 24 months (9.3% & 50.7% respectively). More cases of stunting were reported among males and urban residents (Table 4).

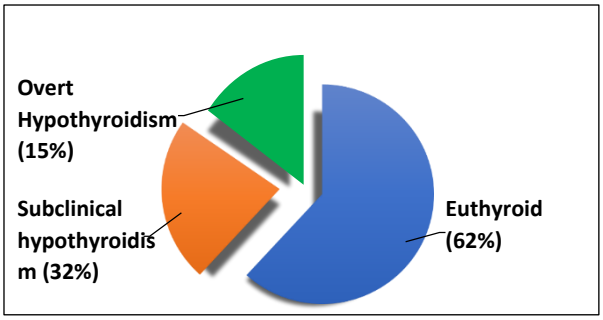

Figure (1): Thyroid function among children with congenital hypothyroidism, Assiut Governorate.

According to thyroid function tests, 15% of children with CH had overt hypothyroidism and 23.0% had

Table (5): Developmental milestones among children with congenital hypothyroidism according to sociodemographic characteristics, Assiut Governorate

Domain	Age Group		Gender		Residence	
	1–< 24 m (*N* = 75)	24–60 m (*N* = 43)	Male (*N* = 56)	female (*N* = 62)	Rural (*N* = 75)	Urban (*N* = 43)
Communication						
Normal = 101	63 84.0%)	38 (88.4%)	47 (83.9)	54 (87.1%)	63 (84.0%)	38 (88.4%)
Delayed = 17	12 (16.0%)	5 (11.6%)	9 (16.1%)	8 (12.9%)	12 (16.0%)	5 (11.6%)
	X^2 = 0.4 *P* = 0.5		X^2 = 0.2 *P* = 0.6		X^2 = 0.4 *P* = 0.5	
Gross Motor						
Normal = 83	42 (56.0%)	41 (95.3%)	39 (69.6%)	44 (71.0%)	8 (18.6%)	35 (81.4%)
Delayed = 35	33 (44.0%)	2 (4.7%)	17 (30.4%)	18 (29.0%)	27 (36.0%)	8 (18.6%)
	X^2 = 20.3 ***P* < 0.001**		X^2 = 0.25 *P* = 0.9		X^2 = 3.9 *P* = 0.06	
	OR = 16.1(3.6–71.5)					
Fine motor						
Normal = 102	62 (82.7%)	40(93.0%)	47(83.9%)	55(88.7%)	63 (84.0%)	39 (90.7%)
Delayed = 16	13 (17.3%)	3 (7.0%)	9 (16.1%)	7 (11.3%)	12 (16.0%)	4 (9.3%)
	***X*² = 2.5** *P* = 0.14		***X*² = 0.6** *P* = 0.4		***X*² = 1.0** *P* = 3.6	
Problem Solving						
Normal=106	67(89.3%)	39(90.7%)	51(91.1%)	55(88.7%)	66(88.0%)	40(93.0%)
Delayed =12	8 (10.7%)	4 (9.3%)	5(8.9%)	7 (11.3%)	9 (12.0%)	3 (7.0%)
	***X*² = 0.6** *P* = 0.8		***X*² = 0.2** *P* = 0.6		***X*² = 0.7** *P* = 0.4	
Personal–social						
Normal=104	65 (86.7%)	39(90.7%)	49(87.5%)	55(88.7%)	64 (85.3%)	40 (93.0%)
Delayed =14	10 (13.3%)	4 (9.3%)	7 (12.5%)	7 (11.3%)	11 (14.7%)	3 (7.0%)
	***X*² = 0.4** *P* = 0.5		***X*² = 0.4** *P* = 0.8		***X*² = 1.5** *P* = 0.2	

Table (6): Growth in children with congenital hypothyroidism according to thyroid function tests, Assiut Governorate

Thyroid Function	weight for age *N* = 118			length /height for age *N* = 118	
	15th–85th percentile *N* = 92 N (%)	< 15th percentile *N* = 17 N (%)	> 85th percentile *N* = 9 N (%)	> 15th percentile *N* = 62 N (%)	< 15th percentile *N* = 56 N (%)
Euthyroid *N* = 73	59 (64.1%)	9 (52.9%)	5 (55.6%)	40 (64.5%)	33 (58.9%)
Subclinical (*N* = 27)	21 (22.8%)	4 (23.5%)	2 (22.2%)	15 (24.2%)	12 (21.4%)
Overt (*N* = 18)	12 (13.0%)	4 (23.5%)	2 (22.2%)	7 (11.3%)	11 (16.7%)
	X^2	1.7		1.6	
	P	0.79		0.45	
Free T4 (mean±SD) p.mol/L	16.7 ± 7.1	14.6 ± 8.9	16.5 ± 9.5	17.35 ± 7.23	15.30 ± 7.73
	ANOVA	*f* = 0.58		*t* = −1.49	
	P	0.7		0.14	
TSH (mean ± SD) µU/ml	8.5 ±13.2	15.3± 29.4	6.5± 13.4	6.4± 9.2	11.3± 19.3
	ANOVA	*f* = 1.1		*t* = 1.8	
	P	0.33		0.08	

subclinical hypothyroidism, whereas the remaining 62.0% showed euthyroid results (Figure 1). Younger children showed significant delays in the gross motor domain. Other developmental delays were also higher among younger children and those residing in rural areas. Developmental delays were

Table (7): Developmental screening results for children with congenital hypothyroidism according to thyroid function tests, Assiut Governorate

Domain	Euthyroid	Subclinical hypothyroidism	Overt hypothyroidism	x^2	P value
	N=73	N=27	N=18		
Communication				38.5	**<0.001**
Normal(n=101)	70 (69.3%)	24 (23.8%)	7 (6.9%)		
Delayed (n=17)	3 (17.6%)	3 (17.6%)	11 (64.8%)		
Gross motor:					
Normal (n=83)	95 (71.1%)	21 (25.3%)	3 (3.6%)	29.4	**<0.001**
Delayed(n=35)	14 (40.0%)	6 (17.1%)	15 (42.9%)		
Fine motor:					
Normal (n=102)	67 (65.7%)	24 (23.5%)	11 (10.8%)	11.7	**0.003**
Delayed (n=16)	6 (37.4%)	3 (18.8%)	7 (43.8%)		
Problem solving:					
Normal (n=106)	67 (63.2%)	25 (23.6%)	14 (13.2%)	3.4	0.18
Delayed (n=12)	6 (50.0%)	2 (16.7%)	4 (33.3%)		
Personal social:					
Normal (n=104)	67 (64.4%)	25 (24.0%)	12 (11.6%)	9.4	**0.009**
Delayed (n=14)	6 (42.9%)	2 (14.2%)	6 (42.9%)		

also higher among boys in all domains except problem solving, where girls displayed more delays. (Table 5).

According to thyroid function tests, neither weight for age nor length/height for age showed statistically significant differences (Table 6).

According to thyroid function tests, overt hypothyroidism showed significantly higher developmental delays in the ASQ3 communication, gross motor, fine motor, and personal–social domains (ORs 37.1, 21.3, 7.1, & 5.6), whereas no statistically significant developmental delays was reported in the problem-solving domain (Table 7).

DISCUSSION

CH is an important disease to study, not only because of its higher prevalence among Middle-Eastern countries including Egypt[23] but more importantly because it is a preventable and treatable cause of intellectual disability with simple cheap and affordable treatment.[7] Among children with CH in this study, the female-to-male ratio was 1.1:1, consistent with meta-analysis finding that pooled female-to-male ratio of CH incidence was 1.3:1[24] and also with previous findings from Fayoum and Zagazig, Egypt,[7,16,25] China,[26] and Shadegan, Arak, and Razavi Khorasan provinces in Iran.[27,28,29] In contrast, boys were more affected than girls in Yazd, Tehran, and Isfahan cities in Iran.[30,31,32] We identified more cases of CH in rural areas, possibly because of higher awareness in urban areas and proper usage of iodized salt, and this finding is consistent with a population-based Iranian study[29]. In contrast, Kshavarziane et al.[27] reported that urban residence was positively associated with CH confirming the effect of urbanization on the high incidence of CH.

TSH is essential for normal growth and development, its action begins in utero, intrauterine thyroid deficiency impairs maturation of the central nervous system and causes loss of interneuron connections,[33] and low TSH is associated with short stature and obesity.[34] We identified here that overweight, and stunting were significantly higher among children with CH and that there was much less underweight among the children who had CH than among the control children. This could be attributable to myxedema caused by CH.

Our results agreed with findings of many studies conducted among children with Children with CH in Egypt and Asia and showed that children with CH had short stature.[35,36,37,38]

Researchers in Iran[39]compared children with CH with a healthy control group and reported no statistical differences in weight and height, although the mean height in the healthy children was higher.

On the contrary, researchers on CH among children admitted to Children's University Hospital in Damascus reported a high weight deficit.[40]

Growth in connection with CH is affected by the child's age at the onset of treatment, which could not be gauged in this study owing to lack of proper recording. In southern Iran, patient height and weight among children who began treatment at age one month or younger and were treated with adequate doses of thyroid replacement therapy grew normally, reaching normal height and weight by age two years.[32] In one study conducted at Insurance Hospital in Ismailia[9], children with CH who were treated showed 20% improvement in weight for age and 26.7% improvement in height for age. Unfortunately, case follow-ups could not be conducted for this study.

Based on ASQ3 scores, children with CH showed delayed developmental milestones on all five domains, which was in agreement with findings from Egyptian and Iranian studies.[35,36]

This finding may be due to the effect of low thyroid hormones (THs) in fetal life which affects brain growth and manifest despite early detection. It was proven that THs effect for brain formation and development begins in utero as THs deficiency during the intrauterine life leads to impaired maturation of the central nervous system and loss of inter neuron connections.[33]

Motor outcome and IQ also correlated with CH severity. For instance, in one study, young adults had persistent cognitive and motor deficits even when CH had been detected by neonatal screening.[41] In another study among patients in a Norwegian neonatal screening program, infants with CH showed delayed motor coordination and global motor proficiency,[42] in a study in Zurich[43], children aged 14 with CH showed worse intellectual outcomes than did the control group. In Minya, Egypt,[44] children with uncontrolled CH showed delayed language, mental, social age, and IQ compared to children with controlled hypothyroidism and normal children.

In contrast to the above findings, researchers in Sohag, Egypt[45], reported no statistically significant differences in history of delayed developmental milestones between children with CH and the control children. Researchers in Ankara, Turkey[46], also reported no differences between children with CH and control children in the personal–social, fine motor, and language domains, although patients with CH showed significantly lower scores for gross motor skills than did the control group.

Researchers in El Sharkia Governorate, Egypt[35], reported highly significant positive correlations between caregivers' compliance with CH treatment and parameters of physical and mental development, but further research is needed to establish the effects of compliance. Unfortunately, compliance could not be monitored in this study because of lack of proper recording.

More cases of overweight and stunting were reported among children with CH younger than 24 months and among boys. Regarding residence, low weight and stunting were higher among children with CH who lived in urban areas, whereas overweight was higher among rural children.

Developmentally, children younger than 24 months with CH showed delays on all five ASQ3 domains, and boys showed greater delays on all domains except problem solving. Children with CH in rural areas also showed greater delays on all domains than did the children in urban areas, possibly because children in urban areas are more likely to attend nursery schools where they gain more skills. This finding aligned with findings from Hamadan province, Iran, that problem solving, and global motor were the domains with the most frequent impairment among girls and boys, respectively.[19] Ehsani et al.[47] also reported abnormalities in fine motor, personal–social, and language among children with CH.

One notable finding from the present study was that thyroid function tests were not significantly associated with growth delay. Heidari et al.[32] confirmed that after treatment began, T4 concentration was associated with increased height, although there was no clear impact of serum TSH concentration on height.

Children with overt hypothyroidism showed statistically significant developmental delays in communication, gross motor, fine motor, and personal social domains. These results conform to the findings from the Egyptian studies conducted in Minya and Sohag Governorates.[44,45] In contrast, Razavi et al.[19] reported no statistically significant differences in developmental delays according to CH severity by thyroid function test results.

CONCLUSION

Despite early diagnosis of CH and initiation of hormone replacement therapy, children with CH showed statistically significant overweight, stunting, and developmental delays compared to normal children. Thyroid function was not significantly associated with growth defects, but children with overt hypothyroid showed significant developmental delay.

Based on the study's findings, several recommendations have been proposed. Accurate monitoring of growth and developmental milestones is essential in all children with CH at every follow-up visit. To overcome the study limitations, proper medical recording procedures should be followed in the form of follow-up cards on children's cases; these cards should be given to caregivers to take home. In this way, medical staff can check on families' compliance with treatment as well as changes in medical history, treatment times, and follow-up periodic thyroid function test results. Finally, future researchers should conduct studies to detect scholastic achievement and IQ among adults with CH, address its effects in other age groups, and explore caregivers' compliance with treatment.

***Limitation of the study*:** Since there is no proper recording system available in health insurance clinic. So, the following data could not be obtained: no follow-up card is given to the children with CH, compliance of treatment and follow-up could not been monitored. No growth monitoring documented. Age at onset of treatment and compliance history cannot be retrieved. Also, No IQ testing was done to children with CH.

Ethical Approval

The study was approved by the Ethical committee of faculty of medicine, Assiut University, Assiut, Egypt

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Declaration of Interest

Authors reported no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions:

Marian Habib, reviewing literature, collection of data, and analysis and interpretation of data, writing discussion; Hala Abou-faddan, choosing the idea and design of study, plan of analysis, and final approval of the version to be published; Kotb Metwalley, preparing and choosing the study tools, revising the scientific issues and final approval of the version to be published; Taghreed Abdul-aziz M Ismail, analysis and interpretation of data, drafting the article and revising it and final approval of the version to be published.

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