Evaluation of thyroid function in children with congenital heart diseases in Assiut University Hospital

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Introduction
Congenital hypothyroidism is one of the preventable causes of neurocognitive impairment because early treatment is possible in neonates. This study was done to assess the prevalence of thyroid function in children with congenital heart diseases (CHD), as many studies have revealed a correlation between CHD and hypothyroidism in children.

Objectives
To assess the prevalence of primary congenital hypothyroidism in patients with CHD.

Patients and methods
The study was conducted on 50 patients with CHD who were systematically examined and screened for thyroid function tests.

Results
The vital signs of cases were within normal range. Pallor was present in 50% of cases with CHD, but no case had jaundice, and 21% of cases had lower limb edema. Approximately 8 and 12% of cases with hypothyroidism showed coarse features and small square hands, respectively, and no cases had mental retardation or hoarseness of voice. Approximately 49.9% of cases of acyanotic group of CHD has cardiomyopathy, 31.5% of cases had heart failure, and 94.6% of cases had a murmur. There were six types of CHD: ventricular septal defect in 37.5% of cases, patent ductus arteriosus in 28.6%, coarctation of aorta in 9.6%, tetralogy of Fallot in 9.6%, and transposition of great arteries in 35%. Seven (14%) cases in our study were diagnosed with congenital hypothyroidism with CHD, and 43 (86%) cases had normal thyroid function. There was no significant difference in anthropometric measures between patients with CHD with hypothyroidism and those with normal thyroid functions. There was no significant difference regarding CHD type, except tetralogy of Fallot, which was presented in 42.8% of patients with hypothyroidism.

Conclusion
Our study assessed the prevalence of congenital hypothyroidism in patients with CHD, as early detection of hypothyroidism helps in early treatment and prevention of neurocognitive impairment.

Keywords:
cardiomyopathy, congenital heart disease, hypothyroidism

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Introduction

Congenital hypothyroidism is one of the most preventable causes of neurocognitive impairment because early treatment is possible in neonates [1]. The thyroid hormone is essential for normal growth and development in infancy [2,3]. The frequency of untreated congenital hypothyroidism has decreased dramatically since the introduction of a national screening test using the capillary thyroid-stimulating hormone (TSH) levels [4]. Congenital heart disease (CHD) is also a risk factor for nonautoimmune hypothyroidism in children [5]. In addition, intravenous iodine contrast media is frequently used as a diagnostic imaging and therapeutic intervention in patients with CHD. Excess iodine exposed to iodine contrast media may disturb thyroid function in adult and pediatric populations [6].

An increased prevalence of thyroid disease, particularly subclinical hypothyroidism, has been reported in Down syndrome. In children with Down syndrome, a possible concomitant subclinical hypothyroidism-related impairment of cardiac function or structure may worsen their clinical condition and ultimately affect their life expectancy [7].

Patients and methods

A cross-sectional study was done at the Pediatric Cardiology Unit of Assiut University Children's Hospital over a 1-year duration between October 2019 and October 2020. The study was conducted on 50 patients with CHD who were examined generally, systematically, and screened for thyroid function tests.

The study has the clinical trial registration number 'NCT03496363.'

Inclusion criteria

Patients diagnosed with CHD, either cyanotic or acyanotic, who were between 2 months and 10 years old were included.

Exclusion criteria

The following were the exclusion criteria:

(1) Cardiac patients with rheumatic heart disease or cardiomyopathy.
(2) Neonates and infants less than 2 months of age.

Methods

All patients were subjected to the following:

Demographic data were collected from parents (name, age, sex, and residence).

(1) Clinical examination, including general and systemic examination
    (a) Vital signs (heart rate, respiratory rate, temperature, and blood pressure).
    (b) Anthropometric measurements (weight, height, head circumference, and abdominal circumference).
    (c) Head and neck examination.
    (d) Hypothyroidism features [coarse facies, abnormal hands (red palms, excessive sweating, and loose nails), depressed nasal bridge, upward slanting eyes, mental retardation, hoarseness of voice, and constipation].
    (e) Skin changes (pallor, cyanosis, jaundice, edema, and presence of scaly skin).
    (f) Systemic (abdominal, chest, cardiac, and neurological) examination.
(2) Investigations:
    (a) Chest radiograph in posteroanterior view.
    (b) Thyroid function tests:
        a. The serum concentration of TSH was directly measured by immunofluorometric assay.
        b. Free T4 was considered a more accurate method of assessing thyroid function using an equilibrium dialysis technique.
    (c) Echocardiography.
    (d) ECG.
(3) Laboratory investigations: TSH and free T4.

Sample collection, storage, and handling

Overall, 3 ml of venous blood was withdrawn under complete aseptic conditions, collected in plain tubes without anticoagulant, and screened for TSH and free T4.

Data collection

(1) Data were collected from the clinical examination of the patients at presentation and at the follow-up, as well as through patients' medical history to calculate the prevalence of hypothyroidism in patients with CHDs.
(2) Computer software SPSS program, version 20, (SPSS: statistical package for social sciences, Chicago,USA) was used for statistical analysis.

Ethical considerations

(1) Approval was obtained from the ethics review committee of Faculty of Medicine, Assiut University.
(2) Verbal and written consents were obtained from all of the caregivers of children with heart failure.
(3) Privacy and confidentiality of all obtained information were observed without intervention in the prescribed treatment.

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Results

Tables 1 and 2 show the vital signs in the examined patients. The mean ± SD blood pressure was 75/51 ± 8/5 in group I and 94/63 ± 7/6 mmHg in group II, the mean ± SD heart rate was 121 ± 26 in group I and 114 ± 20 beat/min in group II, with no significant difference (P = 0.125015). The mean ± SD respiratory rate was 46 ± 12 in group I and 32 ± 8 breath/min in group II, with no significant difference (P = 0.067417).

Table 3 shows that 31% of cases in group I and 19% in group II had pallor. In contrast, no case in both groups had jaundice. Approximately 13% of patients in group I and 9.5% of patients in group II had cyanosis. Lower limb edema was evidenced in 21% in group II, and scaly skin was absent in all cases (Table 4).

Table 5 shows hypothyroidism features in the examined patients.

Table 1 Demographic data of the studied patients

	Total number=50 [*n* (%)]	
Age (years)		
Group I (2 months to 1 year)	31 (62)	
Group II (1 years-10 years)	19 (38)	
Mean±SD	1.39333±9.816	
Sex	Male	Female
Group I (2 months to 1 year)	30%	26%
Group II (1 year-10 years)	24%	20%
Residence		
Rural	39 (78)	
Urban	11 (22)	

Table 6 shows the results of two groups, cyanotic and acyanotic heart disease, based on cardiac examination.

In the cyanotic group, cardiomegaly presented in 50% of cases in group I and 25% in group II, heart failure presented in 16.6% in group I, no abnormal s1 or s2 was seen, and murmur was heard in 75% in group I and 16.6% in group II.

However, in the acyanotic group, cardiomegaly presented in 31.5% of cases in group I and 18.4%in group II, heart failure presented in 21% in group I and 10.5% in group II, no abnormal s1 or s2 was seen, and murmur was heard in 73.6% in group I and 21% in group II (Figs. 1–3).

Table 7 shows six types of CHDs included in the study.

Table 8 shows that the mean ± SD T4 was 1.18 ± 0.37 in group I and 1.079 ± 0.382 in group II. The mean ± SD TSH was 3.319 ± 1.976 in group I and 3.268 ± 2.276 in group II, and seven cases with CHDs of the 50 (14%) cases had hypothyroidism.

Fig. 4 shows that seven (14%) cases in our study were diagnosed with hypothyroidism, and 43 (86%) cases had normal thyroid function (Table 9).

There were no significant differences in anthropometric measurements or vital signs between patients with CHD and hypothyroidism and those with normal thyroid function (Table 10).

Table 2 Vital signs in the studied patients

Groups	BP (mmHg)		HR (beat/min)		RR (cycle/min)	
	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range
Group I (2 months-1 year) *n*=31	75/51±8/5	65/45-90/65	121±26	90-170	46±12	30-70
Group II (1 year-10 years) *n*=19	94/63±7/6	95/55-110/75	114±20	80-50	32±8	20-50
P	0.1356	0.125	0.067			

Table 3 General examination of the studied patients

General examination	Pallor		Jaundice		Cyanosis		Lower limb edema		Scaly skin	
Group I (2 months-1 year) *n*=31	8 (25.8)	23 (74.2)	0	31 (100)	4 (12.9)	27 (87.1)	0	31 (100)	0	31 (100)
Group II (1 year-10 years) *n*=19	4 (21)	15 (79)	0	19 (100)	2 (10.5)	17 (89.5)	4 (21)	15 (79)	0	19 (100)
P	0.703		0		0.401		0.103		0	

Table 4 Anthropometric measures in the studied patients

Anthropometric measures	Weight (kg)		Height (cm)		HC (cm)		Abdominal circumference (cm)	
	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range
Group I (2 months-1 year) *n*=31	6±2	3-11	62±5	53-74	39.5±2	38-44.5	26.23±5.28	24-33
Group II (1yeaar-10 years) *n*=19	13.5±2.5	10-20	88.18±13.80	73-132	48.5±3	45-57	46.47±8.87	33-60

Table 5 Hypothyroidism features in the studied patients

Features of hypothyroidism	Coarse facies		Square hands		Buffy eyes		Depressed nose		MR	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Group I (2 months-1 year) *n*=31	1 (3.2)	30 (96.7)	0	31 (100)	1 (3.2)	30 (96.7)	1 (3.2)	30 (96.7)	0	31 (100)
Group II (1 year-10 years) *n*=19	3 (15.7)	16 (84.3)	2 (10.5)	17 (89.5)	4 (21.05)	15 (78.9)	3 (15.7)	16 (84.3)	0	19 (100)
P	0.1118		0.0226		0.041		0.1118		0	

Table 6 Cardiac examination in the studied patients

Cardiac examination group of patients	Cyanotic (*n*=12)					Acyanotic (*n*=38)				
	Cardiomegaly	HF	Abnormal s1	Abnormal s2	Murmur	Cardiomegaly	HF	Abnormal s1	Abnormal s2	Murmur
Group I (2 months-1 year) *n*=31	6 (50)	2 (16)	0	0	9 (75)	12 (31)	8 (21)	0	0	28 (73)
Group II (1 year-10 years) *n*=19	3 (25)	0	0	0	2 (16)	7 (18)	4 (10)	0	0	8 (21)
Significance	0.161	0.12	0	0	0.004	0.18	0.20	0	0	0.00001

Table 7 Types of congenital heart disease in different age groups

Age groups	VSD	ASD	PDA	COA	TOF	TGA
Group I (2 months-1 year) *n*=31	10 (32.2)	5 (16.1)	4 (12.9)	3 (9.6)	3 (9.6)	6 (19.3)
Group II (1 year-10 years) *n*=19	9 (47.3)	4 (21.05)	3 (15.7)	0	0	3 (15.7)
Significance	0.028	0.659	0.771	0.161	0.161	0.748

ASD, atrial septal defect; COA, coarctation of aorta; PDA, patent ductus arteriosus; TGA, transposition of great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Table 11 shows no significant differences between hypothyroidism and those with normal thyroid function regarding CHD types except for tetralogy of Fallot, which was significantly higher (42.8%) in patients with hypothyroidism ($P = 0.00001$).

ECG was normal in all cases.

Chest radiograph results were normal in 30 cases, bilateral pulmonary consolidation (pneumonia) was present in 17 cases, and pleural effusion was observed in three cases.

Discussion

More than half of the cases in this study (62%) were younger than 1 year, ranging from 1 to 10 years. Males participated in the study at a higher rate than females, and the majority of cases (78%) were from rural areas.

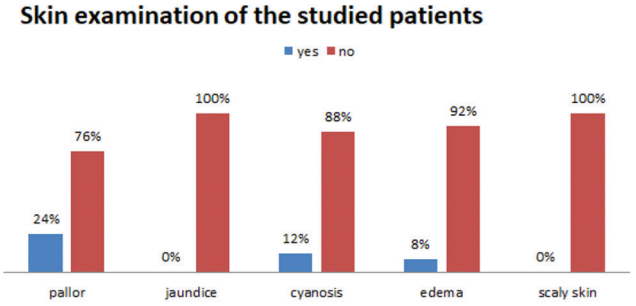
In a previous study by Mıhçı *et al.* [8], in which they evaluated CHD and thyroid abnormalities in children with down syndrome, the female-to-male ratio was 1.08 and the mean age of all of the patients at the time of admission to the health center was 1.57 years (1 day–14.63 year; 1.10–2.03 95% confidence interval of the mean). Of these patients, 164 (87.70%) were younger than 5 years old, 14 (7.49%) were between 6 and 10 years old, and nine (4.81%) were between 11 and 15 years old [8]. However, Lee *et al.* [4] reported that the mean age at initial TFT check-up was 32.2 ± 27.7 (range, 3–98) days after birth, and

Table 8 Thyroid function in the studied patients

Thyroid function	T4 (ng/dl)		TSH (MI U/l)	
	Mean±SD	Range	Mean±SD	Range
Group I (2 months-1 year) *n*=31	1.18±0.4	0.4-1.7	3.32±2	0.5-10
Group II (1 year-10 years) *n*=19	1.079±0.4	0.3-1.7	3.27±2.3	0.5-8.6
Significance	0.24		0.12	

TSH, thyroid-stimulating hormone.

Figure 1



Skin examination of the studied patients.

Table 9 Descriptive data of seven patients with congenital heart disease with hypothyroidism

Demographic and anthropometric					Vital signs			Abnormal features					Type of CHD	
Age (years)	Sex	Weight (kg)	Height (cm)	HC (cm)	BP (mmHg)	HR B/M	RR (cycle/min)	Coarse facies	Square hands	Buffy eyes	Depressed nose	MR	Cyanotic	Acyanotic
4	Male	15	99	49	110/70	90	20	Yes	Yes	Yes	Yes	No	TOF	-
3	Male	13	93	48	100/60	85	23	Yes	Yes	Yes	Yes	No	TOF	-
1	Male	10	85	45	90/55	150	50	No	No	Yes	No	No	TGA	-
6 months	Male	5	64	42	45/65	130	55	No	No	No	No	No	-	PDA
7 months	Male	5	67	43	70/50	150	55	No	No	No	No	No	-	VSD
2	Female	12	85	47	90/55	120	40	Yes	No	Yes	Yes	No	-	ASD
5	Female	18	106	50	100/60	110	20	Yes	No	Yes	Yes	No	TOF	-

ASD, atrial septal defect; CHD, congenital heart disease; PDA, patent ductus arteriosus; TOF, tetralogy of Fallot; TGA, transposition of great arteries; VSD, ventricular septal defect.

Table 10 A comparison between patients with congenital heart disease with hypothyroidism and those with normal thyroid regarding anthropometric and vital signs

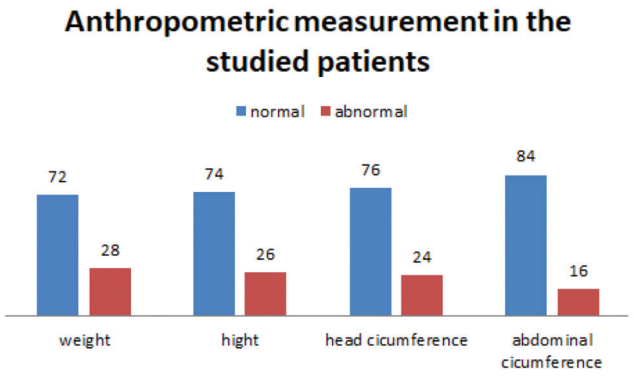
Mean±SD	Age (years)	Weight (kg)	Height (cm)	HC (cm)	HR (b/min)	BP (mmHg)	RR (cycle/min)
patients with hypothyroidism *n*=7	2.29±1.75	11.14±4.8	85.5±15.6	46.2±3.03	119±26.2	86.4/59±22/6.5	37.5±16.3
Patients with normal thyroid *n*=43	2.54±1.84	12.22±5.22	86.44±14.8	47.2±3.53	120±27.4	88.4/60±23/7.5	36.3±15.8
Significance	0.09	1.68	0.125	0.654	0.543	0.0765	0.987

Table 11 A comparison between patients with congenital heart disease with hypothyroidism and those with normal thyroid function regarding the type of congenital heart disease

	VSD	ASD	PDA	COA	TOF	TGA
Patients with hypothyroidism *n*=7	1 (14.2)	1 (14.2)	1 (14.2)	0	3 (42.8)	1 (14.2)
Patients with normal thyroid *n*=43	18 (41.8)	8 (18.6)	6 (13.9)	3 (6.9)	0	8 (18.6)
Significance	0.164	0.779	0.984	0.471	0.00001	0.779

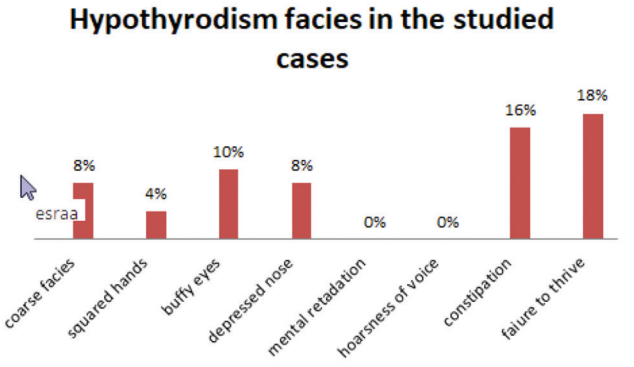
ASD, atrial septal defect; COA, coarctation of aorta; PDA, patent ductus arteriosus; TGA, transposition of great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Figure 2



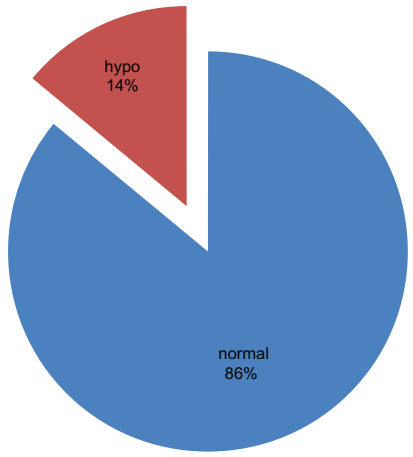
Anthropometric measurements in the studied patients.

Figure 3



Hypothyrodism facies in the studied cases

Figure 4



Thyroid function among the studied patients.

the mean age at the last follow-up was 5.3 ± 2.9 years. Among 36 patients with thyroid dysfunction, 29 (53.7%) infants had transient thyroid dysfunction, and seven (13.0%) patients had permanent hypothyroidism [4].

In the present study,at the time of examination 24% of cases had pallor, 4% had jaundice, and 12% of cases had cyanosis, but edema and scaly skin were not presented in all of the cases.

El-Magd and colleagues previously evaluated the incidence of cardiac abnormalities in children with primary congenital hypothyroidism (PCH). Upon ultrasound or scintigraphy diagnosis, 50 patients with PCH were enrolled (64% had dysgenesis and 36% had dyshormonogenesis). Cardiovascular malformations were present in 18% of all patients, whereas renal anomalies were prevalent in 8%. There was no significant difference in growth and sexual maturation between hypothyroid patients with and without abnormalities throughout a longitudinal follow-up. There was a statistically significant difference between the two groups regarding replacement therapy. Thus, echocardiography should be performed as soon as feasible to test for this birth abnormality and prevent or delay potential problems [9]. According to anthropometric measures in the examined patients. Weight was abnormal in 28%, height was abnormal in 26%, head circumference was abnormal in 24%, and abdominal circumference was abnormal in 14% of cases.

In agreement with our results, El-Magd *et al.* [9] found that ~24% of cases were short (below – 2 SDS), but 76% of cases were within normal height (above – 2 SDS). Delay of the onset of treatment led to retardation of height. Patients diagnosed between 2 years and 6 years and after 6 years were the shortest (mean height SDS=–1.97 and mean height SDS=–1.9, respectively). Patients between 1 month and 2 years of life were shorter (mean height SDS=–1.4), whereas those diagnosed by screening at birth had the best-attended height (mean height SDS=–0.84). Approximately 2% of the studied cases were obese, 4% of cases were overweight, and 94% of cases had a normal BMI [9].

In the present study, according to systemic examination in the studied patients, the cardiac examination was abnormal in all cases, chest examination was abnormal in 10%, abdominal examination was abnormal in 18% of cases, and neurological examination was abnormal in all cases. El-Magd *et al.* [9] supported our study by showing that 6% of cases had a systolic murmur by clinical chest and heart examination.

In the present study, according to investigations done on the studied patients, ECG was normal in all cases; chest radiograph was abnormal in 26%, and echocardiography findings revealed atrial septal defect (ASD) in 18%, ventricular septal defect (VSD) in 38%, coarctation of aorta in 6%, patent ductus arteriosus in 14%, tetralogy of Fallot

in 6%, and finally, transposition of great arteries in 18% [9].

In agreement with our results, El-Magd *et al.* [9] found that 18% of cases had cardiac anomalies in the form of an ASD in four cases, VSD in one case, aortic regurgitation in two cases, pulmonary stenosis in one case, and tricuspid regurgitation in one case. Mıhçı *et al.* [8] reported that the most frequent isolated heart defect was secundum type ASD in 34 (25%) cases, and 41 patients had ASD in association with other cardiac abnormalities. Within this group, 20 also had a VSD (perimembranous and muscular VSD together in the same patient).

Moreover, Lee *et al.* [4] reported that types of CHDs in their patients were as follows: VSD (n = 21), ASD (n = 15), atrioventricular septal defect (n = 1), tetralogy of Fallot (n = 6), pulmonary stenosis (n = 5), Ebstein anomaly (n = 2), functional single ventricle (n = 1), thoracic aorta widening (n = 1), mitral regurgitation (n = 1), and truncus arteriosus (n = 1) [4].

In the present study, hypothyroidism was presented in 14% of cases. Similar to our results, Lee *et al.* [4] reported that 13.0% of their patients had permanent hypothyroidism, Mıhçı *et al.* [8] found 12 (11.88%) cases of congenital hypothyroidism with Down syndrome, of which 11 had CHD. Passeri *et al.* [5] showed that hypothyroidism was diagnosed in 39 (12%) of 324 patients [4,5,8]. Higher than our results, El-Magd *et al.* [9] reported that 50 (100%) children with PCH were included.

Gu *et al.* [10] studied the prevalence of ETA in 1520 Japanese patients with and without Down syndrome. ETA was found in 222 (222/1520) (14.6%) hypothyroid patients without Down syndrome, which was similar to our results, and in 86 (86/1520) (5.7%) patients with Down syndrome by a retrospective review of a questionnaire based on medical records, which were lower than our results [10].

Conclusion

Our study assessed the prevalence of congenital hypothyroidism in CHD, as early detection of hypothyroidism helps in early treatment and prevention of neurocognitive impairment. Our study found that seven patients in the enrolled CHD cases had congenital hypothyroidism.

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Nil.

Conflicts of interest

None declared.

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