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Original article

Thyroid disorders in Libyan patients with Down syndrome

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Abstract

Objective: The association of types of thyroid disorders in Down syndrome patients is well known. Our aim to investigate the thyroid function inLibyan children with Down's syndrome (DS). Methods: Fifty-one Libyan with DS who were followed regularly in our outpatient clinic of endocrine department, Pediatric department, Tripoli University Hospital were studied. There were 37 males and 14 females, with a mean age of 5.7 ± 2.9 years. Originally; were from different Libyan cities, 30 patients from Tripoli (58.8%), 10 from west of Libya (19.6%), 8 from middle of Libya (15.7%) and 3 from south (5.9%). Thyroid function were measured in all DS patients.

Results: In overall regarding thyroid dysfunction, Thirty-Nine subjects DS patients (76%) with thyroid dysfunction. Diagnostic age were ranged from first month of age up to 129 months (10 years) of age. Twenty-two Down syndrome patients (43.1%) diagnosed at first visit. Eleven patients of them (21.5%) of the DS patients presented during first month of age with high level of TSH, diagnosed as congenital hypothyroidism. Furthermore, 9 patients from them with congenital heart disease. Mean age of their mothers 33.4 ± 7.0. 15 mothers their age between 21-29 years and 25 mothers were in third decade of age. Only 11 patients their mother's ≥40 years old,

Conclusions: Thyroid dysfunction is common in Libyan subjects with DS. Children with Down syndrome is very important. Our study would support this recommendation even in children in different of age and without specific thyroid symptom etiology, in particular as they advance in age.

Keywords: Down syndrome, Thyroid function test

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Introduction

The association of types of thyroid disorders in Down syndrome patients is well known. The clinical diagnosis of thyroid disease in young patients is still a difficult problem [1-5]. Many cross-sectional studies in literature from different countries have documented a

prevalence of thyroid abnormalities in pediatric and adults patients with Down's syndrome (DS) varies between 13 - 63% [1, 6-13].

The various thyroid conditions associated with Down syndrome include congenital hypothyroidism, subclinical hypothyroidism, autoimmune hypothyroidism and rarely hyperthyroidism. Subclinical hypothyroidism manifests biochemically as an elevated thyroid-stimulating hormone (TSH) result in the presence of normal thyroxine (T4) and triiodothyronine (T3) and is particularly common in children with Down syndrome.

Since the manifestations of hypothyroidism are nonspecific particularly in infants and may be masked by the features and characteristic of DS, the diagnosis of hypothyroidism in DS largely depends on biochemical results of thyroid function test more than the clinical features of thyroid dysfunction disorder in this group of population. The mean age at diagnosis of hyperthyroidism in Down syndrome was 16.8 years and no female preponderance with the cause is autoimmune, usually Graves Disease [14].Globally, as of 2010, Down syndrome occurs in about 1 per 1,000 births. In Arabic population, the incidence of DS in Kuwait's mixed population is 1.5/1,000 live births, but reaches 3.6/ 1,000 live births among the Kuwaiti population, which is characterized by a high fertility and consanguinity rate [15].

Aim of Study,to assess thyroid dysfunction in Libyan patients with Down syndrome.

Materials and methods: Fifty-one Libyan with DS who were followed regularly in our outpatient clinic of endocrine division, Pediatric department of Tripoli University Hospital, Faculty of Medicine were studied. There were 37 males and 14 females, with a mean age of 5.7 ± 2.9 years. The clinical diagnosis of DS was confirmed by Giemsa banding of chromosomes analysis. Retrospectively we analyzing the medical record for the data at time of presentation (first visit) and the thyroid function tests results. We call all of them for control at time of study for thyroid function assessment in addition to growth parameters assessment.

Laboratory tests

Serum free T4 was measured by the ELISA/competition kit (Enzymon- Test FT4, Boehringer Mannheim, Germany); reference range 12–22 pmol/l. Serum TSH was measured by the ELISA/one-step sandwich kit (Enzymon-Test TSH, Boehringer Mannheim); reference range 0.22–4.2 mU/l, with a lower detection limit of < 0.01 mU/l.

Statistical analysis: The collected data was sorted, coded, then entered and analysed using the SPSS, version 25.0 statistical software.Data were expressed as mean ± SD. Statistical analyses were done using Student's t test. A p value < 0.05 was considered significant.

Results

This study included 51 Libyan children (37 boys and 14 girls) with Down syndrome, and from table (1) we found thatmean age is 5.7 ± 2.9 years old. Mean age of their

mothers 33.4 ± 7.0, 15 mothers their age between 21-29 years and 25 mothers were in third decade of age. Only 11 patients their mother's ≥40 years old. Most of them (58.8%) from Tripoli region and 72.5% were from family with more than sibling (table 1).

Table 1: Demographical and Geographical distribution of DS patients.

Variable	Mean ± SD	
Patient's Age (year)	5.7 ± 2.9	
Mothers' Age	33.4 ± 7.0	
Fathers' Age	39.1 ± 6.6	
Place of residence	n	%
- **West**	10	19.6
- **Capital**	30	58.8
- **South**	3	5.9
- **Middle**	8	15.7
Number of siblings ((brothers and/or sisters))		
- **No**	5	9.8
- **1 – 3**	37	72.5
- **> 3**	9	17.6
Time of diagnosis		
- **At First visit**	22	43.1
- **During follow up time**	17	33.3
- **No thyroid dysfunction**	12	23.5

Eighty-four percent of the DS patients presented to our clinic to start regular follow-up at the first year of age (between one week and 12months of age), and only 15.7% of them presented after the age of 2 years.In overall regarding thyroid dysfunction, 39 DS patients (76%) diagnosed with thyroid dysfunction. The diagnostic age were ranged between first month of age and 129 months (10 years) of age (table 2).

Twenty-two Down syndrome patients (43.1%) diagnosed at first visit, 17 (33.3%) of DS patients diagnosed after the age of 2 years.

Most of the patients with thyroid dysfunction reach to normal thyroid function between 1 month and 3 months after started treatment with L-Thyroxin with increase in their body weight, statically not significant (table 2). In Libya, the neonatal screen for thyroid still not available and not inserted as national screen program yet.

In our study, we observed that 11 patients (21.5%) of the DS patients presented during first month of age with high level of TSH and they diagnosed as congenital hypothyroidism. Furthermore, nine of them have congenital heart disease.

Table 2: Growth parameters of DS patients.

Parameter	First visit		Diagnosis visit		Normalization	
	thyroid dysfunction n= 39	No Diagnosed n= 12	thyroid dysfunction n= 39	No Diagnosed n= 12	thyroid dysfunction n= 39	No diagnosed n= 12
Patient's Age (Months)	8.0 (15)* (0.1 –59)	5.5 (10)* (0.1 – 91)	8.0 (18)* (0.1 – 129)	7.0 (69.75)* (0.1 - 96)	24.0 (36)* (0.2 – 140)	25 (62.8)* (0.8 – 105)
Weight (Kg)	(2.10 – 32 Kg)	(2.70 – 22 Kg)*	(2 –56 Kg)	(10.2 ± 8.7)**	(12.2 ± 6.3)**	(12.5 ± 7.3)**
Height (cm)	(64.3 ± 16.8)**	(62 ± 19.7)**	(65.9 ± 17. 4)**	(71.3 ± 26.2)**	(76.5 ± 18.3)**	(76 ± 22.9)**
BMI	(17.8 ± 5.3)**	(16.2 ±4.2)**	(18.2± 5.1)**	(16.6 ±3.7)**	(19.8 ± 4.4)**	(20.5 ± 4.6)**

At time of diagnosis, most of the Down syndrome patients presented subclinical hypothyroidism with TSH level ≥ 10 and with normal FT4. In addition, 34 patients have congenital heart disease.

Discussion:

Our results showed that 39 Down syndrome patients (76%) diagnosed with thyroid dysfunction, and this diagnostic ranged from first month of age up to 129 months (10 years). These values are higher than that documented in the most of other literature reports, partly due to our diagnostic criteria, which included individuals with only elevated TSH. In literature, Kuwiat study reveals a high frequency of thyroid dysfunction (55%) in DS patients [16]. In addition, many studies [17-19] reported range between 37–66% of thyroid dysfunction in DS patients. The TSH level was significantly higher in the group with primary hypothyroidism compared to the group with subclinical hypothyroidism, but the difference in T4 levels between the two groups was not statistically significant. In our study, we notes that thyroid dysfunction is common in male;, in literature some studies found more hypothyroidism in males [20] but others found more hypothyroidism in females under 20 years of age (21). The relatively high incidence (11 of 51, 21.5%) of congenital hypothyroidism in our cohort of children with Down syndrome has not been reported previously, to the best of our knowledge. This differs greatly from the incidence of congenital hypothyroidism in children with Down syndrome was 28 times higher than that found in the general population [22]. In another study, 1.8 % of 320 children with Down syndrome investigated for thyroid disease were found to have congenital hypothyroidism [23]. In other studies [24-26], the prevalence of congenital hypothyroidism in Down syndrome has ranged from 1.5 to 6.1 %. The

incidence of congenital hypothyroidism in the general population of one in 6,000 by clinical criteria and one in 4,600 by laboratory criteria [27]. The incidence of congenital hypothyroidism in children with Down syndrome is higher than in the general population.

Abnormal TSH levels in children with Down syndrome were noted previously by Samuels et al. [28], their review of 54 such children found ten (19%) of this group to have elevated TSH levels. Furthermore, Subclinical hypothyroidism is very common in children with Down syndrome. The estimated prevalence of subclinical hypothyroidism in the Down syndrome population ranges between 25.3 % [21] and 60 % [29].

In summary, 39/51 (76%) of young children with Down syndrome had significant thyroid disease requiring therapy. Furthermore, 11 of 51 (21.5%) DS patients diagnosed at first month of age considered as congenital hypothyroidism. All DS patients improved clinically with treatment. In our study, we do not diagnosed any case of hyperthyroidism.

Recommendation:

Routine thyroid function screening for all children with Down syndrome is very important. Our study would support this recommendation even in children in different of age and without specific thyroid symptom etiology, in particular as they advance in age.

Limitation of our study, assessment of thyroid antibodies (thyroperoxidase and thyroglobulin), because not available in our hospital as a routine and it is a cost limit. In literature, the presence of thyroid antibodies constitutes a marker for thyroid dysfunction in people with DS

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Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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