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ORIGINAL ARTICLE

Frequency and Risk Factors of Hypothyroidism in Children with Down Syndrome

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ABSTRACT

Objective: To determine the frequency of hypothyroidism in children with Down Syndrome attending out-patients department of National Institute of Child Health, Karachi.
Methods: This cross-sectional study was conducted on Down Syndrome patients visiting for various clinical problems and regular follow-up in outpatient department of National Institute of Child Health, Karachi from 12th September 2016 to 13th March 2017. All children of Down syndrome aged between 1 month to 5 years and of either gender was consecutively enrolled. Venous blood sample was drawn (4 ml) to investigate the T4 and TSH levels. Outcome variable (hypothyroidism) was noted.
Results: Of 104 children, the median age was 2 (1-4) years. There were 58 (56%) females and 46 (44%) males. Mean weight, height and BMI was 10 (6-13) kg, 74 (64-83) cm and 16.6 (14.35-18.30) kg/m^2 respectively. Frequency of hypothyroidism was found in 16 (15.4%) of the children. Hypothyroidism was significantly associated with age (p-value 0.030), BMI (p-value 0.009), and presence of gastrointestinal anomalies (p-value <0.001) of the children.
Conclusion: Hypothyroidism was found considerably higher in our cohort of Down syndrome's children. Moreover, age, BMI and presence of gastrointestinal anomalies were observed as significantly associated determinants.
Keywords: Hypothyroidism, Children, Down Syndrome.

INTRODUCTION

Down syndrome is one of the most prevalent important chromosomal abnormality with an incidence of 1:800 live births.[1] Down syndrome consists of three copies of the q22 long chromosome 21 band constellations, comprising clinical symptoms, as well as biochemical, metabolic and endocrine dysfunctions.[2]
Congenital or acquired, compensated or uncompensated hypothyroidism, transient hypothyroidism or hyperthyroidism, or even persistent hypothyroidism may be the multiple types of thyroid dysfunction in Down syndrome.[3] Studies shows that 3% to 54% of Down Syndrome patients have biochemical evidence of hypothyroidism.[4,5]
As the Down Syndrome patients are developmentally delayed and thyroid hormones have a great impact on brain maturation and IQ level. So, detecting early hypothyroidism in these children significantly improves the mental and functional development of the brain by early addressing the problem. For the same reason, this study was conducted with the aim to determine the frequency of hypothyroidism in patients with Down syndrome attending outpatient department of NICH, Karachi and also to determine the determinants of Down syndrome as well.

METHODS

A descriptive cross-sectional study was conducted after getting approval from College of Physician and Surgeon of Pakistan (CPSP). All Down syndrome children presented with 1

month to 5 years of age visiting for various clinical problems and regular follow up in outpatient department of NICH Hospital, Karachi from 12th September 2016 to 13th March 2017 were enrolled through non-probability consecutive sampling. Patient of Down syndrome already on treatment for hypothyroidism were excluded. While, those having history of thyroid dysfunction in mother, history of birth asphyxia and cerebral palsy were also excluded.

Sample size was calculated taking confidence level: 95%, anticipated population proportion of hypothyroidism in children with down syndrome: 15.6%[6] and absolute precision: 0.07. The estimated sample came out to be 104.

Down Syndrome was defined on the basis of presence of any of three following clinical conditions: Depressed nasal bridge, low set ears, hands are short and broad with short fingers and may have single palmer crease, epicanthic fold (inner corner of eye has rounded fold of skin) and increased gap between 1st and 2nd toe.

Venous blood sample was drawn (4 ml) to investigate the T4 and TSH levels and was checked on standard procedure in atomic energy department Jinnah Post Graduate Medical Centre to avoid the biasness.

Hypothyroidism was labeled as positive on the basis of presence of TSH > 10 mIU/L in infants and > 6.3 in children. T4 < 168 nmol/l in infant and < 172 in children.

For statistical analysis, SPSS version 21 was used. Descriptive statistics included median and interquartile range of continuous data, like age, height, weight and BMI while categorical variables like gender, cardiac anomalies, gastrointestinal anomalies and hypothyroidism were explored through frequencies and percentages. The comparison was also done to see the effect of age, gender, BMI, cardiac anomalies, and gastrointestinal anomalies with hypothyroidism. Chi-square test and Mann-whitney U test was applied. p-value <0.05 was considered significant.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

RESULTS

Out of 104 children with down syndrome, majority (n=63, 60.6%) of the children were presented with ≤2.5 years of age while 41 (39.4%) with >2.5 years of age [median age 2 (1-4) years]. There were 58 (56%) females and 46 (44%) males. Mean weight, height and BMI of the children was 10 (6-13) kg, 74 (64-83) cm and 16.6 (14.35-18.30) kg/m^2 respectively.

Frequency of hypothyroidism was found in 16 (15.4%) of the children. (Figure 1) Comparison of hypothyroidism with respect to baseline characteristics have showed that median age of the children was significantly higher among non-hypothyroidism children than that of hypothyroidism [*2 (1-4) vs. 0.8 (0.2-3.5), p-value* 0.030]. BMI of ≤15 kg/m^2 was significantly higher (n=9, 56.3%) among children hypothyroidism as compared to those without hypothyroidism (n=21, 23.9) (p-value 0.009). Whereas gender (p-value 0.256), weight (p-value 0.214), and height (p-value 0.172) were found to be insignificant. Similarly, comparison of hypothyroidism with anomalies showed significant association with gastrointestinal anomalies (p-value <0.001) whereas cardiac anomalies was found insignificant (p-value 0.655) (Table 1 & 2)

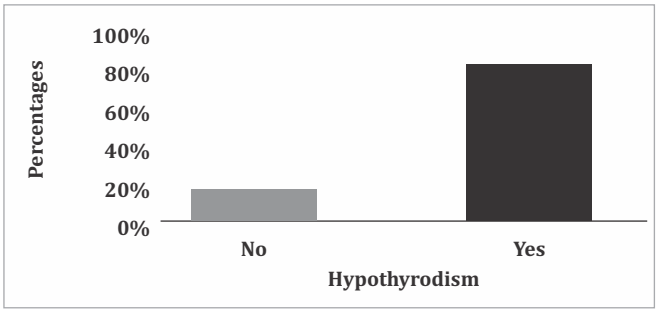

Figure 1: Frequency of hypothyroidism (n=104)

DISCUSSION

The finding of this study revealed that frequency of hypothyroidism was found in higher in children with Down syndrome. Several studies have shown that autoimmune thyroid disorder is more prevalent in patients with Down syndrome.[6-10] Furthermore, it has been revealed that in patients with Down syndrome, the incidence of thyroid peroxidase antibodies was estimated at 7.5-31percent.[10,11]

Table 1: Comparison of hypothyroidism with age and gender of the patients (n=104)

Variables	Hypothyroidism			p-value
	Yes n (%)	No n (%)	Total n (%)	
Age, in years				
≤2.5 years	12 (75)	51 (58)	63 (60.6)	0.199*
>2.5 years	4 (25)	37 (42)	41 (39.4)	
Gender				
Male	11 (68.8)	47 (53.4)	58 (55.8)	0.256*
Female	5 (31.3)	41 (46.6)	46 (44.2)	
BMI, in kg/m²				
≤15 kg/m²	9 (56.3)	21 (23.9)	30 (28.8)	0.009**
>15 kg/m²	7 (43.8)	67 (76.1)	74 (71.2)	
Cardiac Anomalies				
Yes	13 (16.3)	67 (83.8)	80 (76.9)	0.655**
No	3 (12.5)	21 (87.5)	24 (23.1)	
Gastrointestinal Anomalies				
Yes	11 (68.8)	5 (31.3)	16 (15.4)	<0.001**
No	5 (5.7)	83 (94.3)	88 (84.6)	

Chi-square test applied, **Fisher-exact test applied, p-value <0.05 was taken as significant

Table 2: Mean difference of weight, height and BMI among patients with and without hypothyroidism (n=104)

	With Hypothyroidism	Without Hypothyroidism	p-value*
Age, in years	0.8 (0.2-3.5)	2 (1-4)	0.030
Weight, in kg	6.5 (5.25-12.25)	10 (6-13)	0.214
Height, in m	67 (60.5-81.25)	74.5 (64.25-83.5)	0.172
BMI, in kg/m²	14.4 (13.43-18.4)	16.7 (15.1-18.3)	0.141

*Mann-Whitney U test, p-value <0.05 was taken as significant

Similar to our study findings, a study of Shawa CK *et al*, hypothyroidism was seen in 15.6 percent Down syndrome.[12] A longitudinal study indicated that age reduced biochemical deviations. In specific, in the first experiment, more than half of people with subclinical hypothyroidism were normal.[13] In addition, a latest longitudinal study has shown that over a 10-year follow-up period, the incidence of thyroid function in patients with Down syndrome decreased considerably from 90.8 percent to 41.7 percent.[14] Amir Muhammad, *et al* conducted a study for the local prevalence of hypothyroidism in Peshawar. According to the study, the frequency of hypothyroidism in children with Down syndrome is 6 percent in their set up.[15]

In another research, thyroid function of Down syndrome children was evaluated annually, all followed from birth to 10 years of age, congenital hypothyroidism was identified in 7 percent of instances. The likelihood of acquired thyroid dysfunction improved at 10 years from 30

percent at birth to 49 percent. During the follow-up, the subclinical hypothyroidism was almost stable. The likelihood of hypothyroidism improved at 10 years from 7 percent to 24 percent. Study findings showed that the likelihood of enhanced thyroid dysfunction during growth is greater than reported earlier. To recognize thyroid dysfunction early, such kids should be closely tracked annually.[16]

Antibodies to thyroid peroxidase generally occur in late childhood and with age the incidence rises. Some writers indicate that autoimmune hypothyroidism in kids with Down syndrome but rare before this era is prevalent after the era of 8 years.[8,17,18] It is also stated that subclinical primary hypothyroidism is the most common endocrinological pathology associated with Down syndrome. The high frequency of thyroid pathology and diabetes mellitus type 1 in these patients should induce us to have a closer clinical control of children and adolescents with Down syndrome.[19-20]

The findings of this study could be observed in the light of limitation that our study failed to collect data on variables like thyroid gland volume, and its therapeutic outcome. However, in spite of these limitations, our study has provided current magnitude of the problem as no such study has been conducted in recent five years.

CONCLUSION

A high prevalence of hypothyroidism was observed in children with Down Syndrome. In addition, as substantially related factors, age, BMI, and existence of gastrointestinal anomalies were noted. In order to confirm these results, further larger studies are recommended.

AUTHORS' CONTRIBUTION: AA, MK substantially contributed to the conception and design of the study, ER, BN worked in the acquisition, analysis, and interpretation of data. MA drafted the manuscript. AA, MK revised it critically for important intellectual content and gave the final approval of the manuscript.

CONFLICT OF INTEREST: None

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