

Research Article

ASSESSMENT OF THYROID HORMONE ABNORMALITIES IN PATIENTS OF DOWN SYNDROME

SIDDIQUI MH¹, IQBAL W², RANA MA³, SUFIYAN M⁴, SALEEM FSM⁴, PERVAIZ R^{*4}

¹Department of medicine and endocrinology, Akhtar Saeed medical and dental college Lahore, Pakistan

²Vice Principal, Red Crescent Medical and Dental College, Lahore

³Department of Critical Care Medicine, Amna Inayat Medical College & Bahria International Hospital, Lahore, Pakistan

⁴Department of Medicine and Critical Care, Bahria International Hospital, Lahore, Pakistan

*Corresponding author email: drizwanperwaiz@gmail.com



Keywords

Down syndrome, Thyroid dysfunction, Euthyroid, Hypothyroidism, Hyperthyroidism, Sick thyroid syndrome,

Abstract: Down syndrome is the fourth most common syndrome caused by chromosomal abnormalities. This syndrome includes many abnormalities such as thyroid hormone dysfunction. The current study was designed to determine the prevalence of thyroid dysfunction in clinically diagnosed cases of Down syndrome patients that were confirmed on karyotyping later before including in the study. This Cross-sectional study was carried out at different Hospitals of Lahore to find out the prevalence of thyroid hormone dysfunction in 50 clinically diagnosed Down syndrome (DS) subjects from September 2019 to May 2021 by measuring thyroid function tests (T3, T4, TSH), and antithyroid antibodies (ATA). A total 50 Down syndrome cases were included in the study and majority of the patients were males 33(66.0%) while 17(34.0%) were females. Thyroid dysfunction was found in 27 (54%) of DS subjects, of whom 13 (26.0%) had hypothyroidism, 08 (16.0%) were having subclinical hypothyroidism, 01 (2.0%) had sick thyroid syndrome, 4 (8.0%) were hyperthyroid and 01 (2.0%) was subclinical hyperthyroid. ATA was positive in 07 (14.0%) patients of DS, of whom 02 (28%) were males and 05 were females (72%), 03 had hypothyroidism, 02 had hyperthyroidism, 02 had subclinical hypothyroidism. remaining 23 (46.0%) were having euthyroid status. This study showed that 54% of Down syndrome patients that were clinically diagnosed had thyroid hormone dysfunction. It can be concluded that thyroid hormone dysfunction is found in high prevalence in DS patients.

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Introduction

Down syndrome is typically caused by a mistake in cell division called non-disjunction. The non-differentiation results in one embryo with three copies of chromosome 21 instead of the usual two. Before or at conception, a pair of chromosomes 21 within the sperm or egg does not separate. As the embryo develops, the extra chromosome is replicated in every cell of the body. Down syndrome is the fourth most common genetic disorder worldwide (Albert, 2018; Cipriani et al., 2018). Worldwide Prevalence of Down syndrome is 1 out of 700-1000, live births which are 0.1%. (Pierce et al., 2017) There are three types of Down syndrome including 95% Nondisjunction, 2-4% Mosaicism and 2-6% Translocation. The Frequency of DS increases with increasing maternal age, oxidative stress, Alcohol, smoking at time of pregnancy, consanguineous marriages, certain diets, air

pollutions, decrease levels of (selenium, vitamin E, vitamin C, vitamin A, uric acid, Glutathione). Even very young mothers, maternal irradiation, fertility drugs, oral contraceptives, low folate levels, elevated plasma homocysteine levels and spermicides, phenylalanine hydroxylase activity impairment and over activity of DYRK1A Kinase may have a chance of a child with DS (Abdulrazzaq et al., 2018). There are 6 million worldwide and 40000 people in USA are living with Down syndrome. According to CDC, nearly 5500-6,000 babies are born in USA with Down syndrome per year. (Mohan et al., 2018; Purdy et al., 2014; Sinai et al., 2018)

13-50% of Down syndrome cases are found to be associated with thyroid disorders (Smith, 2001). Subjects with Down syndrome (DS) are at increased risk for the development of all forms of thyroid disease:

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Hypothyroidism, Subclinical hypothyroidism, Sick thyroid syndrome, hyperthyroidism and subclinical hyperthyroidism (Pierce et al., 2017).

Thyroid dysfunction in Down syndrome ranges from subclinical hypothyroidism (60-63%) to hypothyroidism (19.2%), sick thyroid syndrome, autoimmune thyroiditis (6.5-34%), and hyperthyroidism 4.1% The autoimmune thyroid disease (Hashimoto’s thyroiditis 13-34% and Graves’ disease 1.3-6.5%) with Down syndrome have a higher prevalence than in general population.(Aversa et al., 2015). Frequency of thyroid diseases in patients with Down syndrome, starting in newborn population is 0.7-1%, in children 3-54% and in adults, it is 12-30%. The American Academy of Pediatrics (AAP) advise a screening protocol for thyroid function tests T3, T4, TSH and antithyroid antibodies in children with DS. This should be done at birth, at 6 months, 1 year, and annually up to the age of 21 in order to avoid severe consequences like irreversible brain damage. (Ayub et al., 2017; Purdy et al., 2014) Amniocentesis is done from 15 to 20 weeks of gestation, while chorionic villus sampling from 9 to 14 weeks. Karyotyping chromosomal analysis is done to confirm the diagnosis. (Mohan et al., 2018) Signs and symptoms of hypothyroidism can be difficult to discriminate from those found in the natural course of DS itself. (Purdy et al., 2014) No such study regarding association and prevalence of thyroid disorder in subjects with Down syndrome has been found in Pakistan. So, the aim of the current analysis is to assess the ratio of thyroid dysfunction in DS patients.

Material and methods

In this cross-sectional survey, purposive sampling technique was used. Sample size was calculated to be 50 through online calculator (2003-2005) on the basis of prevalence 24% of thyroid dysfunction (Pierce et al., 2017) in patients with Down syndrome by using

10%confidence interval and 90%confidence level. Patients with Down syndrome, both male and female were included, and Current use of thyroxin or anti-thyroid hormone were excluded. Questionnaires were used for data collection development from literature review and expert opinion. For data collection Consent was obtained from parents of all participants of study and permission was taken from institute. A diagnosis of Down syndrome is typically confirmed through genetic testing, such as a karyotype test or chromosomal microarray analysis, which can detect the presence of an extra copy of chromosome 21. However, we included the patients who showed any of the physical characteristics of Down syndrome such as a flattened facial profile, a small nose and upward slanting eyes, a small head and short neck, a single crease across the center of the palm, poor muscle tone and loose joints, a shorter than average height, and a tongue that protrudes slightly from the mouth.

Measurement of T3 and T4:

The individuals were tested for thyroid dysfunction. 5-10 ml venous Blood was drawn and collected in a vacutainer from patients with Down syndrome by using standard protocols. Thyroid function tests including serum or plasma T3 and T4 determinations were made by chemiluminescent competitive immunoassay technique, similarly the Thyroid stimulating hormone (TSH) was measured by the standard methods used in the biochemistry laboratory. For statistical analysis SPSS version 23 was used and p value less than 0.05 was considered statistically significant.

Results

A total of fifty Down syndrome diagnosed cases were analyzed for thyroid hormones levels. The male to female ratio was 33:17. Table one showed the variation of thyroid hormone, thyroid stimulation hormones and anti-thyroid antibodies levels in Down syndromes patients.

Table 1 Levels of thyroid hormones in Down syndrome patients

Variables	Ranges of variables	Male n (%)	Female n (%)	P-value
T3 ng/ml	<i>Normal 0.80-1.79</i>	24 (48)	8 (16)	0.098
	<i>Below 0.80</i>	8 (16)	6 (12)	
	<i>Above 1.79</i>	1 (2)	3 (6)	
T4 µg/dl	<i>Normal 6.00-12.19</i>	24 (48)	8 (16)	0.098
	<i>Below 6.00</i>	8 (16)	6 (12)	
	<i>Above 12.19</i>	1 (2)	3 (6)	
TSH µIU/ml	<i>Normal 0.34-5.59</i>	2 (4)	3 (6)	0.011
	<i>Below 0.34</i>	2 (4)	4 (8)	
	<i>Above 5.59</i>	11 (22)	10 (20)	

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ATA	NA	20 (40)	3 (6)	0.07
	Positive	2 (4)	5 (10)	
	Negative	11(22)	9 (18)	
Antithyroid antibodies (ATA), T3= Triiodothyronine., T4= Thyroxine, TSH= Thyroid stimulating hormone, P-value of TSH was found 0.011 among Male and Female, which is significant statistically				

Table 2 Shows Thyroid Function in children with Down syndrome

Variables	Male n (%)	Female n (%)
Euthyroidism	20(40)	3(6)
Hypothyroidism	7(14)	6(12)
Subclinical Hypothyroidism	4(8)	4(8)
Sick thyroid syndrome	1(2)	0(0)
Hyperthyroidism	1(2)	3(6)
Subclinical Hyperthyroidism	0(0)	1(2)

The table above shows that the frequency of thyroid dysfunction in DS patients was 27(54%).

Discussion

A total of 50 children of DS were included in the study and majority of the children were Males 33(66.0%) while remaining proportion 17(34.0%) was Female. Vallani et al.,2016 showed 59% males and 38% females which is compatible to our study.(Villani et al., 2016)

Our study showed that among 50 children of Down syndrome, 46(92.0%) were having non-dysfunctional and 4(8%) Translocation types of DS. Study was presented by Asim et al., 2015 who reflected that 96-98% had non-dysfunctional and 2-4% Translocation types of DS which are comparable to our work.(Asim et al., 2015)

Our study showed that among 50 children of Down syndrome, 07(14.0%) were positive for antithyroid antibodies. Aversa et al.,2015 revealed in study that 6-34 % had positive Antithyroid antibodies (ATA) which are comparable to our thesis work.(Aversa et al., 2015)

Our study reflected that among 50 children of Down syndrome, 13(26.0%) were hypothyroid. The results of our study are comparable with the study done by Capone et al., 2018 who confirmed that 27% had hypothyroidism. (13) Our study showed that among 50 children of Down syndrome, 08(16.0%) had Subclinical hypothyroidism. Similar results were presented by Purdy et al., 2014 who confirmed that 15% had Subclinical hypothyroidism.(Purdy et al., 2014) Our study elucidated that among 50 children of Down syndrome, 01(2.0%) were having Sick thyroid syndrome. Similar results were described by Purdy et al., 2014 depicted that 2.5% had Sick thyroid syndrome.

Our study showed that among 50 children of Down syndrome, 4(8.0%) had Hyperthyroidism. Aversa et al., 2015 in study reflected that 4.1% were Hyperthyroid which is comparable to our study (Aversa et al., 2015).

Our study reflected that among 50 children of Down syndrome, 01(2.0%) were having Subclinical hyperthyroidism. Tüysüz & Beker, 2001 demonstrated in study that 2(0.62%) had Subclinical hyperthyroidism which is comparable to our study (Tüysüz and Beker, 2001).

Our study showed that among 50 children of Down syndrome, 27(54%) had Thyroid dysfunction in DS subjects. Ayub et al., 2017 asserted in study that 3-54% had Thyroid dysfunction which is compatible to our research work.(Ayub et al., 2017)

Conclusion

Thyroid dysfunctions were found as frequent endocrine disorders associated with Down syndrome subjects including Hypothyroidism, Subclinical hypothyroidism, Sick thyroid syndrome, Hyperthyroidism, and Subclinical hyperthyroidism respectively.

Conflict of Interest

The authors declared an absence of conflict of interest.

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