

**University of Alttahadi**

**Faculty of pharmacy**

Project title

**Incidence Of Hypothyroidism and Cardiac Diseases Among Libyan Down Syndrome Patients**

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**(**وَلَمَّا بَلَغَ أَشُدَّهُ وَاسْتَوَى آتَيْنَاهُ حُكْمًا وَعِلْمًا وَكَذَلِكَ نَجْزِي الْمُحْسِنِينَ**)**

سورة القصص

الآية 14

# DEDICATION

*To set an example of the poor and sincere approach to personnel secretary Guide to humans to the beloved heart and soul to the joy of the Messenger of Allah peace be upon him.*

*To the source of giving and compassion to the mystery out of my life to chest, who warmth and it includes to make us forget the fatigue and misery to from this moment waited impatiently for my*

***Beloved mother.***

*To the blood that is in our veins to her our love of life, love and safety we ask God to protect her and bond us*

***Sister***

*To struggled with them along the paths of science and lived with them moments will remain forever in my mind and my heart*

***Dear friends.***

*To lighting us roads and have been credited to reach this level*

***Distinguished Professors.***

*All of them dedicate the fruit of this effort.*

*God grants success*

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# ABSTRACT

**Background**. Subclinical hypothyroidism (SCH) is the commonest thyroid abnormality in patients with Down syndrome (DS). The purpose of this study was to determine incidence rate of hypothyroidism and cardiac defects among pediatric down syndrome patients in Libya.

**Methodology**. A retrospective study was conducted in children with 50 DS seen at endocrine follow-up clinic in Tripoli university hospital. Data were collected from patients' registration book and medical records.

**Results**. A total of 50 patients with DS were included in the study out of which 64% were females. Their median age at diagnosis was range between 10–14 years. Abnormal thyroid function was observed in 34 patients (68 %). Presence of chronic heart disease were seen in 30(60%) patients.

**Conclusion.** Thyroid abnormalities were seen in a remarkable proportion of DS patients. Early diagnosis and management of thyroid abnormalities are important to decrease further impairment of cognition function in children with DS.

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# CHAPTER 1

# INTRODUCTION

## 1.1 Down syndrome

Down syndrome is a chromosomal condition that is associated with intellectual disability, a characteristic facial appearance, and weak muscle tone (hypotonia) in infancy. All affected individuals experience cognitive delays, but the intellectual disability is usually mild to moderate

People with Down syndrome often have a characteristic facial appearance that includes a flattened appearance to the face, outside corners of the eyes that point upward (upslanting palpebral fissures), small ears, a short neck, and a tongue that tends to stick out of the mouth. Affected individuals may have a variety of birth defects. Many people with Down syndrome have small hands and feet and a single crease across the palms of the hands. About half of all affected children are born with a heart defect. Digestive abnormalities, such as a blockage of the intestine, are less common.

Individuals with Down syndrome have an increased risk of developing several medical conditions. These include gastroesophageal reflux, which is a backflow of acidic stomach contents into the esophagus, and celiac disease, which is an intolerance of a wheat protein called gluten. About 15 percent of people with Down syndrome have an underactive thyroid gland (hypothyroidism). The thyroid gland is a butterfly-shaped organ in the lower neck that produces hormones. Individuals with Down syndrome also have an increased risk of hearing and vision problems. Additionally, a small percentage of children with Down syndrome develop cancer of blood-forming cells (leukemia).

Delayed development and behavioral problems are often reported in children with Down syndrome. Affected individuals can have growth problems and their speech and language develop later and more slowly than in children without Down syndrome.

Additionally, speech may be difficult to understand in individuals with Down syndrome.

Behavioral issues can include attention problems, obsessive/compulsive behavior, and stubbornness or tantrums. A small percentage of people with Down syndrome are also diagnosed with developmental conditions called autism spectrum disorders, which affect communication and social interaction.

People with Down syndrome often experience a gradual decline in thinking ability (cognition) as they age, usually starting around age 50. Down syndrome is also associated with an increased risk of developing Alzheimer's disease, a brain disorder that results in a gradual loss of memory, judgment, and ability to function. Approximately half of adults with Down syndrome develop Alzheimer's disease. Although Alzheimer's disease is usually a disorder that occurs in older adults, people with Down syndrome commonly develop this condition earlier, in their fifties or sixties.

## 1.2 Causes

Most cases of Down syndrome result from trisomy 21, which means each cell in the body has three copies of chromosome 21 instead of the usual two copies.

Less commonly, Down syndrome occurs when part of chromosome 21 becomes attached (translocated) to another chromosome during the formation of reproductive cells (eggs and sperm) in a parent or very early in fetal development. Affected people have two normal copies of chromosome 21 plus extra material from chromosome 21 attached to another chromosome, resulting in three copies of genetic material from chromosome 21. Affected individuals with this genetic change are said to have translocation Down syndrome.

A very small percentage of people with Down syndrome have an extra copy of chromosome 21 in only some of the body's cells. In these people, the condition is called mosaic Down syndrome.

Researchers believe that having extra copies of genes on chromosome 21 disrupts the course of normal development, causing the characteristic features of Down syndrome and the increased risk of health problems associated with this condition.

Hypothyroidism is a clinical disorder commonly encountered by the primary care physician. Untreated hypothyroidism can contribute to hypertension, dyslipidaemia, infertility, cognitive impairment, and neuromuscular dysfunction. Data derived from the National Health and Nutrition Examination Survey suggest that about one in 300 persons in the United States has hypothyroidism. The prevalence increases with age, and is higher in females than in males. Hypothyroidism may occur as a result of primary gland failure or insufficient thyroid gland stimulation by the hypothalamus or pituitary gland. Autoimmune thyroid disease is the most common aetiology of hypothyroidism in the United States. Clinical symptoms of hypothyroidism are nonspecific and may be subtle, especially in older persons. The best laboratory assessment of thyroid function is a serum thyroid-stimulating hormone test. There is no evidence that screening asymptomatic adults improves outcomes. In the majority of patients, alleviation of symptoms can be accomplished through oral administration of synthetic levothyroxine, and most patients will require lifelong therapy. Combination triiodothyronine/thyroxine therapy has no advantages over thyroxine monotherapy and is not recommended. Among patients with subclinical hypothyroidism, those at greater risk of progressing to clinical disease, and who may be considered for therapy, include patients with thyroid-stimulating hormone levels greater than 10 mIU/l and those who have elevated thyroid peroxidase antibody titres.

***1. Primary hypothyroidism:***

This type of hypothyroidism results of intrinsic disorder of thyroid gland, upon biochemistry lab test (thyroid function test) show serum thyroxin (T4) is Low and Thyroid Stimulating Hormone (TSH) is elevated. The most common cause of primary hypothyroidism is deficiency of the element iodine. In the US, the most common cause is destruction of the thyroid gland by the immune system, a condition called Hashimoto's thyroiditis

***2. Secondary hypothyroidism:***

This type is rare, is due to pituitary or hypothalamic failure, results failure in Thyroid Stimulating Hormone (TSH) secretion.  
Biochemistry lab test result (thyroid function test) show serum thyroxin (T4) is Low and Thyroid Stimulating Hormone (TSH) is Low.

## 1.3. Type of hypothyroidism:

In hypothyroidism, two main types describe this clinic state:

1. ***Congenital hypothyroidism:***

About 90% of hypothyroidism in pediatric is congenital, and results from dysgenesis of thyroid gland, and may be permanent or transient state.

1. ***Subclinical hypothyroidism:***

is defined as serum levels of TSH above the upper limit of the reference range, in the presence of normal concentrations of total T4 or free T4, diagnosed more frequently in clinical practice in young and middle-aged, this biochemical profile might be an indication of mild hypothyroidism, and may classified as autoimmune and non-autoimmune according presence or absence of thyroid antibodies. (2)

## 1.4 Common cardiac diseases associated with down syndrome:

Cardiovascular disease is a leading cause of morbidity and mortality in individuals with Down syndrome. Congenital heart disease is the most common cardiovascular condition in this group, present in up to 50% of people with Down syndrome and contributing to poor outcomes. Additional factors contributing to cardiovascular outcomes include pulmonary hypertension; coexistent pulmonary, endocrine, and metabolic diseases; and risk factors for atherosclerotic disease. Moreover, disparities in the cardiovascular care of people with Down syndrome compared with the general population, which vary across different geographies and health care systems, further contribute to cardiovascular mortality; this issue is often overlooked by the wider medical community. This review focuses on the diagnosis, prevalence, and management of cardiovascular disease encountered in people with Down syndrome and summarizes available evidence in 10 key areas relating to Down syndrome and cardiac disease, from prenatal diagnosis to disparities in care in areas of differing resource availability. All specialists and nonspecialist clinicians providing care for people with Down syndrome should be aware of best clinical practice in all aspects of care of this distinct population.(3)

## 1.5 Aim of study:

The aim of my object is to determine incidence rate of hypothyroidism and cardiac defects among pediatric down syndrome patients in Libya.

# 

# CHAPTER 2

# MATERIALS AND METHODS

Data of 50 down syndrome patients were collected at pediatric endocrine out patient department in Tripoli university hospital.

Collected data included age, gender, thyroid function test results and types of cardiac problems and organized as table then results were analyzed using excel program to calculate percentage of each, figures were done by excel program.

# CHAPTER 3

# RESULTS

Collected data were organized in table 1, sequence of patients was random based on first collected.

Patient’s age was grouped into four groups, among all patients age were of higher number in age group from 10- 14 years old and their percentage were 50% of all patients, then age group from 5-9 years old with percentage 28%, age group from 0-4 years represents 14% of all cases and lastly 8% for age group 15-18 years old.

**Table 1. Age related characteristics**

|  |  |  |
| --- | --- | --- |
| Age group | No. of patients | Percentage |
| 0-4 years | 7 | 14% |
| 5- 9 years | 14 | 28% |
| 10- 14 years | 25 | 50% |
| 15- 18 years | 4 | 8% |

Figure 1: age groups of 50 dawn syndrome patients

Dawn syndrome is more common in female than male, percentage of patient were 64% compared to 36% for male patient.

Figure 2: patient’s gender

Based on collected data, 14% of DS patients were presented with normal thyroid function test (7 patients), 10% showed clinical hypothyroidism (5 patients), 4% with non-significant results were TSH results were normal while T3 or T4 were high (2 patients), most of cases included in this study showed subclinical laboratory test results where TSH was high and T3 or T4 results were normal (54% of patients, no. of cases 27 patients), 12% of our data were missed data (6 patients).

Table 3. TFT results

|  |  |  |
| --- | --- | --- |
| TFT results | No. of patients | Percentage |
| Normal TSH and Normal T3 or T4 | 7 | 14% |
| High TSH and High T3 or T4 | 5 | 10% |
| Normal TSH and High T3 or T4 | 2 | 4% |
| High TSH and Normal T3 or T4 | 27 | 54% |
| Missed data | 6 | 12% |

Figure 3: shows results of thyroid function test

For cardiac problem groups, 60% of our patient were diagnosis with cardiac disease none of diagnosis patient were excluded and 40% of them no data found in their files about Echo results.

Table 4. Association between CHD and down syndrome

|  |  |  |
| --- | --- | --- |
| Presence of CHD | No. of patients | Percentage |
| Yes | 30 | 60% |
| No | None | None |
| Missed data | 20 | 40% |

Figure 4: type of cardiac problem associated with dawn syndrome

# CHAPTER 4.

# DISCUSSION

## 5.1 Discussions

Down syndrome (DS) is associated with several medical conditions and one of which is thyroid abnormalities (4). There is a higher risk of thyroid function deterioration over time in patients with DS which seems to be related to higher baseline TSH levels at diagnosis and autoimmunity. However, hypothyroidism in DS appears to be unrelated to autoimmunity (5).

DS is usually associated with extra-thyroidal autoimmunity than thyroid autoimmunity.27-29 Regardless of the underlying causes, untreated hypothyroidism may aggravate growth and development retardation in patients with DS during infancy and childhood (6).

Thyroid hormones are vital hormones essential for the central nervous system, particularly during infancy (6). The physical signs and symptoms of hypothyroidism overlap with DS. Hence, hypothyroidism may not be considered in infants with DS. This observation leads to have a regular screening of DS patients for possible thyroid abnormalities

There is a wide range of prevalence of thyroid abnormalities in DS patients which can be explained by the variability in the definition of thyroid disorders, the different population size or the age of patients studied and by the different techniques used to measure the TFT in different studies.11 In the current study, thyroid abnormalities were detected in 34 patients (68 %), which was higher than studies done in other countries like South Africa (34.5%), California (32.5%) and Oregon (24%) (6-8). Though, they recommend screening for thyroid abnormalities in DS patients at birth, 6 months, 12 months, and yearly then after, [4] in the present study, a significant number of thyroid abnormalities were detected between 10- 14 years of age. This might result in increased prevalence of thyroid abnormalities in the current study compared with the above studies. Other studies also recommend to have additional testing between 2 and 6 months of age (6). Therefore, we propose additional screening in children with DS for thyroid abnormalities in order to detect the abnormalities earlier and to start treatment timely.

For cardiac problem groups, 60% of our patients were diagnosed with cardiac disease which represents only the data found; so, for this limitation, education for physicians regarding importance of better documentation to obtain a realistic data in the next study.

## 5.2 Conclusion

In conclusion, thyroid abnormalities were seen in a high proportion of down syndrome patients in our study which calls for placement of regular screening of patients with down syndrome for thyroid abnormalities. Patients with down syndrome should be screened also for other common co-morbidities and linked to respective referral clinics timely to decrease impairment of cognition and improve their quality of life.

## 5.3 Limitation

This study was limited by missed data in files of included patients where most of files were inorganized and results of cardiac echo was not found and even if results mentioned it was not specified based on type of cardiac disease of concern.

## 5.4 Future work

* Awareness program regarding age of patient’s mother at time of birth.
* Screening of genetic defective gene in relatives before marriage.

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