ORIGINAL ARTICLE

# HYPOTHYROIDISM IN CHILDREN WITH DOWN'S SYNDROME: A HOSPITAL BASED STUDY

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## ABSTRACT

**Background:** Children with Down's syndrome have a high incidence of associated treatable medical disorders. Hypothyroidism occurs with increased frequency in individuals with Down's syndrome. The objective of this study was to determine the frequency of hypothyroidism in children with Down's syndrome. **Methods:** This study was conducted at Department of Pediatrics, Lady Reading Hospital, Peshawar, from October 2006 to September 2007, on 50 children with Down's syndrome to find out the frequency of hypothyroidism. Thyroid function tests were performed in all these children. **Results:** Among 50 children with Down's syndrome 30(60%) were males and 20(40%) females. Age of majority 21(42%) was less than 1 year in 18(36%) cases age ranged from 1-5 years with mean age of 3.1291$\pm$3.65 years. Majority of the patient's mothers 17 (34%) were in the age range of 31-35 years. Frequency of hypothyroidism was found to be 3 (6%). **Conclusion:** Frequency of hypothyroidism in children with Down's syndrome is 6%.

**KEY WORDS:** Down's syndrome, Hypothyroidism, Thyroid function tests.

## INTRODUCTION

Down's syndrome (DS) (trisomy 21, mongolism) is the most frequent trisomy in humans[1] and is perhaps the oldest recognized condition associated with mental retardation and developmental delay.[2] In 1866, Down's described clinical characteristics of the syndrome that now bears his name.[3] DS is more likely to occur at older maternal age.[4,5] Mothers under 25 years of age known to have the average risk of DS pregnancy of 1:1600, rising to 1: 350 at 35 and 1:40 at age 43.[6]

The cause of Down's syndrome is full trisomy 21 resulting from non-disjunction in 95% of cases,[7] while mosaicism (2.4%) and translocation (3.3%) account for remainder of cases.[5,8] The presence of an extra copy of the proximal part of q21, q22 appears to result in the typical physical phenotype of mental retardation, brachycephaly, hypotonia, flat facies, slanted palpebral fissures, epicanthic folds, brush field spots on the iris, relatively large protruding tongue, small low set ears and hand anomalies (short and broad hand, clino-dactyly of the fifth finger, Simian crease).[5,8] Congenital heart defects, seizures, strabismus, nystagmus, atlantoaxial instability, cryptorchidism, increased risk of leukemia, dementia, duodenal atresia and hypothyroidism are usually associated with Down's syndrome. Down's syndrome is therefore easily diagnosed by recognition of dysmorphic features and distinctive phenotype shortly after birth.[5,8]

Children with DS have a high incidence of associated treatable medical disorders where early intervention carries a better outcome.[9]

Hypothyroidism occurs with great frequency in individual with Down's syndrome.[10,11] Therefore, thyroid function test should be a part of an annual preventive medical screening for each individual with Down's syndrome.[12] However some young children with Down's syndrome run abnormally high TSH level which subsequently normalize; therefore high TSH alone does not necessarily predict incipient hypothyroidism, but these individuals should be kept under close surveillance.[13]

Down's syndrome is a common chromosomal anomaly associated with hypothyroidism and other congenital abnormalities, which are the leading cause of mortality in these children. It is important to identify individuals with Down's syndrome who have thyroid disorder since hypothyroidism may compromise normal central nervous system functioning.

The objective of this study was to determine the frequency of hypothyroidism in children with Down's syndrome.

## MATERIAL AND METHODS

This descriptive study was conducted in the Paediatrics Department, Postgraduate Medical Institute, Lady Reading Hospital Peshawar, for one year from October 2006 to September 2007. A total of 50 children [born in Khyber Pukhtoon Khwa (KPK)] clinically recognized as having Down's syndrome presented to Paediatrics unit, Lady Read-

ing Hospital Peshawar were included in the study by convenient (non-probability) sampling technique. Patients with dysmorphic features other than Down's syndrome were excluded from the study. The exact maternal age was recorded. Detailed history of every child was taken. The child was first assessed (via physical examination) for Down's syndrome based upon the typical clinical features of the syndrome. The Physical findings to look in these children include: mongoloid facies, brachycephaly, depressed nasal bridge, protruding tongue, small low set ears, upward slanted eyes with epicanthal fold, short neck, short and broad hands, transverse single palmar crease, hypotonia and delayed milestones.

All these children then underwent thyroid function tests including T3, T4, TSH, carried out by ELISA. All the information was recorded on a proforma.

Mean ± standard deviation was calculated for quantitative variables like age and mother age. For gender, male to female ratio was calculated. The results were presented through Tables. The data was stored and analyzed by SPSS version 12.0.

## RESULTS

During the study period 50 cases of Down's syndrome were admitted; 30 (60%) males and 20 (40%) females with male to female ratio of 1.5:1.

Among these 50, 3 (6%) patients were found to have hypothyroidism.

Patients were divided into various age groups. Most of the patients, 21 (42%) were in the age group less than 1 year, followed by 18 (36%) in the age group 1-5 years, 9 (18%) in of 6-11 years and 2 (4%) in the age group of 11-15 years. Minimum age was 5 days and maximum 14 years with mean age of 3.1291±3.65 years.

Majority of the patient's mothers 17 (34%) were in the age range of 31-35 years, with mean age of 33.34±5.88. (Table 1)

## DISCUSSION

The average age at presentation in our patients with Down's syndrome was 3.12 years (range 5 days to 16 years). Almost same results are reported in a study conducted in Northeast Malaysia.[14]

Inheritance of DS is still not completely understood. However, earlier workers strongly advocated that the advanced maternal age is a major risk factor for trisomy 21. The likelihood that a woman under 25 and 30 years who becomes pregnant will have a baby with DS is less than 1 in 1,400 and 1,000 respectively.[15] Chance of having a baby with DS increases to 1 in 350 for women who become pregnant at the age 35 and continues to increase as the woman ages, so that by age 42, and by age 49, the chance is 1 in 60 and 1 in 12 respectively.[15] On the contrary there are reports that 80% of DS babies are born to young women of age less than 30 years.[15]

More than 50% babies with DS are born to women of advanced maternal age (AMA) (> 35 years). The prevalence of DS pregnancies varies with maternal age. The risk rises from under 1:1,000 live births in women under 25 years to approximately 1% at age 40 years and 7% at 48 years. In a study the mothers' ages at the birth of the child with DS ranged from 18 to 45 years, and 21 (42%) were of AMA.[16] In our study advanced maternal

**Table 1: Age range of patients with Down's syndrome and their mothers (n=50).**

| Features | Number of Patients | Percentage | Mean ± SD |
|---|---|---|---|
| **Age Range of patients (in years)** | | | |
| Less than 1 year | 21 | 42% | |
| 1 - 5 years | 18 | 36% | 3.12±3.65 |
| 6 - 10 years | 9 | 18% | |
| 11 – 15 years | 2 | 4% | |
| **Age Range of mother (in years)** | | | |
| 15 - 20 years | 1 | 2% | |
| 21 - 25 years | 2 | 4% | |
| 26 - 30 years | 14 | 28% | 33.34±5.88 |
| 31 - 35 years | 17 | 34% | |
| 36 – 40 years | 12 | 24% | |
| 41 – 45 years | 4 | 8% | |

age was found in approximately 32% cases. So our results are in agreement with the results of the study mentioned above.[16] While in another study with regard to maternal age, 64% of the mothers were older than 35 years of age, while the remaining 36% of mothers were less than 35 years of age at the time of birth of the affected child. Average maternal age at birth of the affected child was 32.3 (range 21–50) years.[14]

Even though there are over 50 clinical symptoms of DS, it is rare to find all or most of them in one person.[15] The clinical diagnosis of Down's syndrome usually presents with no particular difficulty. The diagnostic accuracy of Down's syndrome on the basis of clinical features in the neonatal period has been reported to range from 73% to 100%.[21] Nevertheless, even an experienced physician may find it occasionally difficult to give a confirmatory diagnosis on an infant when the clinical features may be minimal. Karyotyping is essential for confirmation of the clinical diagnosis, determination of recurrent risk and to provide a basis for genetic counseling. Although the particular karyotype responsible for Down's syndrome has little, if any, effect on the phenotype of the patient, it is essential for determining the risk of recurrence.[14]

In our study craniofacial features were the foremost indicators of clinical suspicion of Down's syndrome. Among the craniofacial features studied, appearance (mongoloid facies), head (microcephalic brachycephalic) eyes (upward slanted, epicanthal folds) were the most frequent feature observed in all (100%) cases. The other major clinical features present in our patients with Down's syndrome were; nose (short with depressed nasal bridge) in 96% cases, development (delayed milestone) in 92% cases, extremities (short and broad hand with incurved little finger, transverse single palmar crease, wide gap between the big and second toe) in 86% cases, neuromuscular (generalized hypotonia) in 76% cases, neck (short and broad) in 74% cases, tongue (protruding) in 64% cases, abdomen (protuberant, umbilical hernia) in 38% cases. More or less same observations of clinical features are also reported in some national and international studies.[14,17,18]

There is an unexplained higher incidence of congenital hypothyroidism (CH) detected by T4-based neonatal screening programs and a very high prevalence of (mild) plasma TSH elevation in young children with Down's syndrome.[11] In an observational study to determine whether newborns with DS have decreased blood T4 concentrations at the time of the neonatal screening, a large and representative cohort of Dutch children with Down's syndrome born in 1996 and 1997 were studied. T4, TSH, and T4-binding globulin concentrations were analyzed in comparison with clinical information obtained by interviewing the parents and data from the general newborn population and a large control group. The mean T4 concentration of the studied children with DS (n=284) was significantly decreased. The individual T4 concentrations were normally (Gaussian) distributed but shifted to lower concentrations. This could not be explained by prematurity, non-thyroidal illness, or iodine exposure. Mean TSH and T4-binding globulin concentrations were significantly increased and normal, respectively. The decreased T4 concentration, left-shifted normal distribution, and mildly elevated TSH concentrations point to a mild hypothyroid state in newborns with DS and support the existence of a DS-specific thyroid disorder.[11]

In this study thyroid function test was done in all children with Down's syndrome. TSH was normal in 94% cases while it was high in 06% cases. T3 and T4 were normal in 96% cases and these were low in 4% cases respectively and on the basis of these results we encountered hypothyroidism in 6% cases presented with Down's syndrome during our study period. As some feature of hypothyroidism mixed with Down's syndrome and hypothyroidism is also found in Down's syndrome so it is recommended that thyroid function test must be done in all patients with Down's syndrome and the need for adequate treatment of its dysfunction. Thus, the symptoms of the disease would be alleviated and better physical and mental development ensured. Limitations of the study were its small sample size and hospital based study. A large scale study at the provincial level need to be done to know the exact frequency of hypothyroidism in children with Down's syndrome.

## CONCLUSIONS

The frequency of hypothyroidism in children with Down's syndrome is 6% in our set up.

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