

Patterns Of Autoimmune Diseases Among Yemeni Children with Down Syndrome

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Abstract

Background: Down syndrome can be associated with autoimmune diseases such as Celiac disease, autoimmune Thyroiditis, Type 1 DM and other diseases. **Aim:** The aim of this study was to determine the prevalence of hypothyroidism, Type 1 DM, and Celiac disease in Yemeni children with Down syndrome as well as the most common mother's age for the occurrence of this syndrome. **Method:** This study was cross-sectional study involving one hundred and six Yemeni children with Down syndrome selected by simple random sampling from Special Needs Centers for Down syndrome in Sana'a city, Yemen, during 2019. These children were investigated for the presence of anti-thyroid peroxidase antibodies, TSH, and T4 for hypothyroidism; random blood sugar, anti-glutamic acid decarboxylase antibodies for Type 1 DM; and antitransglutaminase immunoglobulin A, and G antibodies for Celiac disease. **Results:** The prevalence of autoimmune diseases in the 106 Yemeni children with Down syndrome was 5.77% hypothyroidism, 2.8% Type 1 DM, and 0.94% Celiac disease. The highest number of Down syndrome babies were born at 41 to 50 years of mother's age. **Conclusion:** Hypothyroidism was the most prevalent autoimmune disease in Yemeni children with Down syndrome and Celiac disease was the least prevalent. Down syndrome can occur at any maternal age, but may increase with age. Children suffering from Down syndrome should be monitored periodically for autoimmune diseases to make early diagnosis, start early treatment, and decrease the occurrence of complications.

Keywords: Autoimmune diseases; Down syndrome, Hypothyroidism, Type 1 DM, Celiac disease, Yemeni children

I. INTRODUCTION

Down syndrome (DS), or trisomy 21, represents the most common chromosomal abnormality associated with intellectual impairment [1]. Down syndrome is the most common chromosomal disorder with prevalence estimates ranging from 6.1 to 13.1 per 10,000 people [2,3]. Most often DS results from complete trisomy of chromosome 21, due to non-disjunction during gamete formation (about 95%), while the remaining ones are due to either complete or partial translocation of chromosome 21 to another chromosome, typically in the D (13–15) or G (21–22) group [4]. Down syndrome is the most common recognizable genetic syndrome associated with abnormal immune function and immune defects. Individuals with DS have a higher incidence of autoimmune disorders [5]. The increased susceptibility to

infections has been associated with atypical immune function in conjunction with various non-immune related medical and anatomical comorbidities [6]. Among those, endocrinopathies are the most common [7]. The physiopathological bases for these changes are not fully understood, and studies suggest that endocrine dysfunction in DS may be multifactorial explained not only by autoimmunity but also by cellular mechanisms [8]. To the best of our knowledge, there is no previous study in Yemen about prevalence of autoimmune diseases among Down syndrome individuals, also there is a wide variation in reported prevalence rates of autoimmune diseases in other countries among Down syndrome individuals compared to general population, so the aim of this study was to determine the prevalence of hypothyroidism, Type 1 DM, and Celiac disease in Yemeni children with Down syndrome as well as the most common mother's age for the occurrence of this syndrome.

II. SUBJECTS AND METHODS

The present study was a cross-sectional study, carried out on 106 Yemeni children with Down syndrome (60 male and 46 female), aged 5 to 18 years, selected mainly from Special Needs Centers for Down's syndrome in Sana'a city, Yemen, during 2019. Sample size was calculated by using OpenEpi program (Version 2.3.1) using 95% confident level, expected frequency of Down syndrome is 13.1% according to De Graaf [2], target children number 220, design effect 1 and sampling was done by simple random sampling. The study was approved by the committee of Postgraduate Studies and Scientific Research of the Faculty of Medicine and Health Sciences, Sana'a University. Written informed consent was obtained from parents of participant prior to enrolling them in the study. Six ml of venous blood was collected from each participant into labeled plain test tubes for determination of random blood sugar for diagnosis diabetes mellitus by using Cobas Integra 400 plus auto-analyzer (Roche, Germany), serum thyroid-stimulating hormone (TSH), Free thyroxin (FT4) using Cobas E411 auto-analyzer (Roche, Germany), anti-thyroid peroxidase antibodies for diagnosis of thyroid disorders, anti-transglutaminase IgA, IgG for diagnosis of Celiac disease, and anti-glutamic acid decarboxylase (anti-

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GAD) for diagnosis of Type 1 DM by Snibe Maglumi 4000 plus Immunoassay Analyzer (Snibe Diagnostic, China).

Statistical analysis

The results were analyzed by Social Package of Statistical Science (SPSS) version 21 (LEAD Technologies; Inc. USA) to get frequencies, percentage, mean and standard deviation.

Results

The mean age of participants was 10.5 ± 3.4 years and mean body mass index (BMI) was 17.6 ± 4.8 kg/m². The prevalence of autoimmune diseases in Down syndrome children is shown in table 1. Among all children with Down syndrome only six children, 3 males and 3 females (5.66%) had positive antibodies against thyroid peroxidase (TPO), and high TSH with low T4, three children, 1 male & 2 females (2.8%) had positive antibodies against ant glutamic acid decarboxylase (anti-GAD) with a random blood sugar >200 mg/dl. Positive anti-transglutaminase of IgG class was found in one child (0.94%).

1. Table (1): Clinical characteristics of Down syndrome individuals

Variables	Prevalence
Hashimoto Thyroiditis	5.66 %
Type 1 DM	2.8 %
Celiac disease	0.94 %

Table 2 shows the distribution of Down syndrome babies according to maternal age at birth. Although Down syndrome can occur at any maternal age, but the highest number of down syndrome babies were born to women at the age of 41 to 50.

Table (2): Distribution of Down syndrome baby numbers according to maternal age at birth

Maternal age	Number of Children	Percentage
20 - 30 (years)	8	7.6%
31 - 40 (years)	33	31.4%
41 - 50 (years)	50	47.7%
51 - 60 (years)	14	13.3%

III. DISCUSSION

Down syndrome can be associated with autoimmune diseases such as Celiac disease, autoimmune thyroiditis, and Type I DM [9-12], because Down syndrome individuals have abnormal expression of the autoimmune regulator (AIRE) gene that is located on chromosome 21 (21q22.3 region) and has been identified as a likely cause for increased autoimmunity in Down syndrome, because the AIRE gene regulates T-cell function and self-recognition, so abnormal AIRE expression in children with Down syndrome may increase autoimmunity [13,14]. This study reported that female children with Down

syndrome had higher prevalence of Type 1 DM compared to males (66.7% vs. 33.3%). In general, the increased susceptibility of female to autoimmune diseases may be attributed to chromosomal factors, such as skewed Xchromosome inactivation [15] or to female sex steroids [16]. The overall prevalence of Type 1 DM in Yemeni children with Down syndrome was 2.77%, which is less than the prevalence of Type 1 DM in Emirati children with Down syndrome (4.3%) [17]. The prevalence of hypothyroidism (Hashimoto Thyroiditis) in Yemeni children with Down syndrome was 5.77%, which is less than the prevalence of hypothyroidism in Emirati children with Down syndrome (19.6%) [17]. The prevalence of Celiac disease in this study was 0.94%, which is less than that in the Arab world that lies between 2% and 3.8% [18,19].

The highest number of Down syndrome babies were born at 41 to 50 years of mother's age because nondisjunction of chromosomes can occur during either meiosis I or meiosis II of oocytes and increases with increased maternal age that lead to increase chromosomal abnormalities [20,21].

IV. CONCLUSION

Hypothyroidism was the most prevalent autoimmune disease in Yemeni children with Down syndrome, followed by Type 1 DM and then Celiac disease being the least prevalent autoimmune disease. Down syndrome can occur at any maternal age, but may increase with maternal age. Children suffering from Down syndrome should be monitored periodically for autoimmune diseases for early diagnosis, start early treatment, and decrease the occurrence of complications.

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VI. DECLARATIONS

No conflict of interest is associated with this work.

VII. REFERENCES

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