Original Article

Prevalence and impact of endocrinopathies on growth in pediatric down syndrome patients

A retrospective analysis

Ahmed M. Al Qassimi, *MBBS, MD,* ***Rayan A. Al Marzooq,*** *MD,* ***Lena H. Alfaraj,*** *MD,* ***Nafisah M. Al Radhwan,*** *MD,* ***Zainab A. Al-Askari,*** *MD,* ***Ahmed S. AlKhalifah,*** *MD.*

ABSTRACT

الأهداف: تقييم انتشار أمراض الغدد الصماء وتأثيرها على النمو لدى الأطفال المصابين بمتلازمة داون في المنطقة الشرقية بالمملكة العربية السعودية.

المنهجية: أجريت دراسة استرجاعية مقطعية في مستشفى القطيف المركزي بين يناير 2015م وديسمبر 2022م. تم تحليل بيانات 358 طفلًا مصابًا بمتلازمة داون (تتراوح أعمارهم بين 0–14 سنة)، بما في ذلك البيانات السريرية والأنثروبومترية والمخبرية. تم تقييم معدلات انتشار أمراض الغدد الصماء وعلاقتها بالأمراض المصاحبة وتأثيرها على مقاييس النمو باستخدام الأساليب الإحصائية.

النتائج: كان قصور الغدة الدرقية هو الأكثر شيوعًا (18.9%)، يليه نقص فيتامين د (15.4%). وُجدت ارتباطات ذات دلالة إحصائية بين قصور الغدة الدرقية والسمنة (p=0.009 ونقص فيتامين د (p=0.000). وكان تأخر النمو شائعًا، مع انحرافات ملحوظة في درجات Z للطول والوزن بين المرضى المصابين بقصور الغدة الدرقية ونقص فيتامين د وانقطاع النفس الانسدادي أثناء النوم (p<0.05).

الخلاصة: أمراض الغدد الصماء شائعة بين الأطفال المصابين بمتلازمة داون، وتؤثر بشكل كبير على النمو والنتائج الصحية. يعد الفحص المبكر والعلاج متعدد التخصصات ضروريين لتحسين الرعاية الصحية.

Objectives: To assess the prevalence of endocrinopathies and their impact on growth among pediatric patients with Down syndrome (DS) in the Eastern Region of Saudi Arabia.

Methods: This study utilized a retrospective cross-sectional design and was conducted at the Qatif Central Hospital between January 2015 and December 2022. Data from 358 pediatric patients with DS (aged 0–14 years), including clinical, anthropometric, and laboratory findings, were analyzed. The prevalence rates of endocrinopathies, their association with comorbidities, and their impact on growth metrics were evaluated using statistical methods.

Results: Hypothyroidism was the most prevalent endocrinopathy (18.9%), followed by vitamin D deficiency (15.4%). Significant associations were observed between hypothyroidism and obesity (p=0.009), as well as vitamin D deficiency (p<0.001). Growth impairment was common, with notable deviations in height and weight Z-scores among patients with hypothyroidism, vitamin D deficiency, and obstructive sleep apnea (p<0.05).

Conclusion: Endocrinopathies are common among children with DS and substantially affect growth and health outcomes. Early screening and multidisciplinary management strategies are essential to improve patient care.

Keywords: Down syndrome, endocrinopathies, hypothyroidism, growth impairment, vitamin D deficiency, Saudi Arabia

Saudi Med J 2025; Vol. 46 (4): 364-371
doi: 10.15537/smj.2025.46.4.20241117

From the Pediatric Department, Qatif Central Hospital, Al Qatif, Kingdom of Saudi Arabia.

Received 4th November 2024. Accepted 17th March 2025.

Address correspondence and reprint request to: Dr. Ahmed Mohammed Al Qassimi, Pediatric Department, Qatif Central Hospital, Al Qatif, Kingdom of Saudi Arabia. E-mail: amq7872030@gmail.com
ORCID ID: https://orcid.org/0009-0007-7511-3682

Down syndrome (DS) is a genetic condition that results from having an additional chromosome 21, typically resulting from non-disjunction during meiosis, Robertsonian translocation, or mosaicism. In Saudi Arabia, a study conducted in Riyadh reported a DS prevalence of approximately 1.8 for every 1,000 live births.[1] Down syndrome affects multiple organ systems,

leading to complications such as congenital heart defects, gastrointestinal abnormalities, and endocrine, hematological, neurological, musculoskeletal, ophthalmological, and otorhinolaryngological disorders. Therefore, comprehensive screening is essential to prevent long-term complications that may affect growth and overall health.[1]

Significant growth disparities have been observed between children with and without DS, particularly from birth to five years of age.[2] Endocrinopathies, including type 1 diabetes mellitus, hypothyroidism, obesity, and short stature, are more prevalent among individuals with DS.[3] In response to these findings, an updated growth chart specific to DS was released in 2015, providing healthcare professionals with improved tools to monitor growth in this population. These growth conditions and endocrinopathies not only affect physical development, but also influence body mass and physical activity, due to factors such as muscular hypotonia and obesity, further compounding the risk of endocrine complications.

In addition to endocrinopathies, autoimmune diseases are notably more prevalent in patients with DS, with common conditions including thyroid disorders, gastrointestinal autoimmune diseases, and islet cell autoimmunity.[3-5] This heightened autoimmune activity reflects a more aggressive autoimmune phenotype in children with DS.[6,7] A study on autoimmune thyroid disorders (AITDs) also highlighted that children and adolescents with AITDs are at increased risk of developing additional autoimmune conditions, such as alopecia areata, vitiligo, and celiac disease.[7]

Thyroid dysfunction in individuals with DS tends to occur earlier and more frequently than in the general population. However, most cases of hypothyroidism observed in DS are transient and unrelated to autoimmunity. Therefore, routine testing for antithyroid antibodies is recommended only in selected cases.[8] A multi-institutional registry study on thyroid disorders in patients with DS revealed that most patients were diagnosed with hypothyroidism before visiting DS specialty clinics, highlighting the importance of these clinics in providing up-to-date healthcare management and early diagnosis of thyroid disorders.[8] The American Academy of Pediatrics (AAP) advises regular screening for thyroid dysfunction at crucial life stages, at birth, at 6 months, at 12 months, and once a year thereafter, to enable early detection and effective management.[9]

Despite extensive global research on DS, there is a notable lack of studies addressing endocrinopathies and their impact on growth in Saudi Arabia and other similar regions. Understanding the local prevalence and clinical implications of these conditions is crucial for developing healthcare protocols tailored to the needs of this population. To address this gap, this study, conducted at the Qatif Central Hospital (QCH), aimed to assess the prevalence of endocrinopathies in patients with DS and evaluate their impact on growth. Additionally, it sought to explore the association between these endocrinopathies and other comorbid conditions. The primary objective of this study was to determine the prevalence of various endocrinopathies and their clinical significance in patients with DS within this regional context.

Methods. This study employed an observational, analytical, cross-sectional, retrospective design to investigate the prevalence and impact of endocrinopathies on the growth of pediatric patients with DS at QCH in the Eastern region of Saudi Arabia. This study was approved by the Qatif Central Hospital Research and Institutional Review Board (IRB). The selected study design allowed for the assessment of prevalence and clinical associations in a defined population over a specific timeframe using pre-existing medical records. The cross-sectional design enabled the identification of the associations between endocrinopathies and growth outcomes without requiring long-term follow-up, making it well-suited to the study objectives. Consent was waived as the data were retrospectively collected from existing medical records, as approved by the IRB.

Data were retrospectively extracted from electronic health records and patients' physical medical files. The study population comprised pediatric patients aged 0–14 years who were diagnosed with DS and exhibited clinical or laboratory evidence of endocrinopathy. Patients were excluded if they had incomplete medical records, were lost to follow-up, or showed no evidence of endocrinopathy, resulting in a final sample size of 358. Although no formal power calculation was performed, the sample size represented the entire eligible population from medical records and provided a robust dataset for the exploratory analysis of endocrinopathies and growth outcomes in patients with DS.

Data integrity and privacy. To minimize bias and ensure data accuracy, no alterations were made to the medical records collected during the analysis. Personal identifiers were removed to maintain patient

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

confidentiality, and each participant was assigned a unique identification code. All data were securely stored in a password-protected electronic file accessible only to the primary investigator.

Variables and data management. The research gathered a diverse set of variables, comprising demographic details such as age, gender, and date of birth; anthropometric measurements (weight, height, and body mass index [BMI]); diagnostic details (including the type of endocrinopathy and date of diagnosis); comorbidities; and laboratory markers of autoimmune activity, such as antinuclear antibody, anti–Saccharomyces cerevisiae antibodies, and antineutrophil cytoplasmic antibodies. The data were compiled into an Excel spreadsheet for preliminary review and cleaning, followed by coding for statistical analysis.

Growth assessment and Z-scores. In this study, the CDC Z-scores were used for the average population rather than the CDC centiles for patients with DS. This method enabled a straightforward comparison of the growth measurements between patients with DS and the broader population. The CDC Z-scores provide a standardized reference, enabling the identification of deviations and identify specific growth impacts attributable to endocrinopathies in patients with DS. This method ensures that the growth retardation or acceleration observed in patients with DS is quantified against a universally accepted growth standard, facilitating the recognition of significant clinical deviations and informing targeted interventions.

Statistical analysis. The analysis was performed using Python 3.7. Descriptive statistics, including medians and interquartile ranges, were computed for continuous variables, while categorical variables were represented using frequencies and percentages. The Mann-Whitney U and Kruskal-Wallis H tests were utilized for continuous variables comparison among groups due to the data's non-normal distribution, while the Chi-square test was employed for categorical variables. A *p*-value less than 0.05 along with a 95% confidence interval was deemed to be statistically significant.

Results. This study examined the occurrence and features of endocrinopathies in individuals with DS, along with their effects on growth and overall health. These findings highlight the significant prevalence of endocrinopathies in patients with DS, emphasizing the elevated risk of autoimmune and metabolic complications.

Baseline characteristics. Among the 358 patients with DS included in this study, the majority (94.5%) were of Saudi Arabian descent, and 52.5% were male. Most patients were born at 38 gestational weeks, with a median birth height of 49 cm, positioning males at the 5th percentile and females below the 5th percentile according to DS growth charts. The median birth weight was 2.9 kg, which was slightly above the 25th percentile for both genders. Table 1 provides a detailed breakdown of baseline characteristics, including age, current height, weight, BMI, family history of DS, and endocrinopathies.

Prevalence of endocrinopathies. Hypothyroidism was the most prevalent endocrinopathy observed, affecting 18.9% of patients. Subclinical hypothyroidism was observed in 10.81%, congenital hypothyroidism in 2.7%, and acquired hypothyroidism in 5.4% of the cohort. Vitamin D deficiency was documented in 15.4% of patients with DS. Other notable endocrinopathies included obesity (3.1%), hyperlipidemia (1.2%), and type 1 diabetes mellitus (0.4%).

Comorbidities. This study revealed a high prevalence of congenital heart defects (32.8%), intellectual disabilities (7.7%), developmental delays (7%), and structural gastrointestinal abnormalities (4.3%) in the DS population. Additionally, 2.7% of patients were diagnosed with obstructive sleep apnea (OSA), and recurrent respiratory infections were common.

Table 1 - Baseline features of patients with Down syndrome.

Characteristic	Median (IQR)
Age (months)	72.00 (23.00-135.00)
Current height (cm)	102.00 (82.00-130.00)
Current weight (kg)	17.00 (10.00-35.00)
Body mass index (kg/m^2)	16.76 (14.18-20.90)
Height Z-score	-2.0 (-3.0--1.0)
Weight Z-score	-1.0 (-2.5-0.0)
Body mass index Z-score	-1.0 (-2.0-0.5)
Birth height (cm)	49.00 (48.00-50.00)
Birth weight (kg)	2.90 (2.50-3.15)
Gestational age (weeks)	38.00 (38.00 - 38.00)
Endocrinology follow-up per year	1.00 (1.00 - 1.00)
	n (%)
Gender (male)	136 (52.5%)
Saudi nationality	245 (94.6%)
Consanguinity between parents	
None	20 (7.7%)
First degree	7 (2.7%)
Second degree	4 (1.54%)
Unknown	228 (88.0%)
Family history of Down syndrome	
True	249 (96.1%)
False	10 (3.9%)
Family history of endocrinopathies	
True	252 (97.3%)
False	7 (2.7%)

IQR: interquartile range

Associations with endocrinopathies. Significant associations were observed between hypothyroidism and several variables, including consanguinity between parents (p=0.037), family history of endocrinopathies (p=0.026), vitamin D deficiency (p<0.001), dyslipidemia (p=0.022), thyroid peroxidase antibodies (p=0.035), and obesity according to BMI (p=0.009). These associations are summarized in Table 2. Furthermore, vitamin D deficiency was significantly associated with hypothyroidism (p<0.001), acquired hypothyroidism (p<0.001), developmental delay (p=0.002), intellectual disability (p=0.005), OSA (p=0.012), and IgA deficiency (p=0.023). These associations are presented in Table 3.

Impact on growth. Growth metrics, as measured by Z-scores, showed significant differences depending on the presence of endocrinopathies and comorbidities. Patients with obesity, subclinical hypothyroidism, acquired hypothyroidism, vitamin D deficiency, and OSA had significantly higher median weight Z-scores than those without these conditions (p<0.05). In contrast, patients with congenital heart defects exhibited a notably lower weight Z-score of -1.5 (p=0.02). Additionally, obese patients had significantly lower height Z-scores (p<0.001). Body mass index Z-scores were notably higher in patients with subclinical hypothyroidism, acquired hypothyroidism, vitamin D deficiency, and OSA (p<0.05). Table 4 outlines these findings in detail.

Routine follow-up and screening. Routine follow-ups in the DS clinic facilitated the screening and timely diagnosis of various endocrinopathies. The median age at diagnosis of hypothyroidism was 4 years, whereas type 1 diabetes mellitus and obesity were typically diagnosed by 9 years. A significant association was observed between consanguinity, a family history of endocrinopathies, and various forms of hypothyroidism (p=0.004 and p=0.026, respectively). Additionally, a family history of endocrinopathies was significantly associated with hypertriglyceridemia (p=0.027) and obesity (p=0.043), emphasizing the influence of genetic factors in the inheritance of endocrinopathies (Table 2).

Vitamin D deficiency. Vitamin D deficiency was found in 15.4% of the patients, with significant associations observed with comorbid conditions such as intellectual disability (p=0.004), developmental delay (p=0.001), and IgA deficiency (p=0.019). These findings suggest that vitamin D deficiency is a common and impactful condition in patients with DS, and contributes to additional health complications. Other antibodies, such as anti-thyroglobulin antibodies and thyroid peroxidase, yielded insignificant results, likely

Table 2 - Associations with hypothyroidism (n=49).

Variable	True n (%)	False n (%)	*P*-value
Consanguinity between parents	5 (45.45%)	44 (17.74%)	0.037
Family history of endocrinopathies	4 (57.14%)	45 (17.86%)	0.026
Vitamin D deficiency	18 (45%)	31 (14.16%)	<0.001
Dyslipidemia	3 (75%)	46 (18.04%)	0.022
Thyroid peroxidase antibodies	2 (100%)	47 (18.29%)	0.035
Obesity according to body mass index	12 (37.5%)	37 (16.3%)	0.009

The percentages in the table represent the proportion of Down syndrome (DS) children within each condition who have hypothyroidism (True) compared to those without hypothyroidism (False). Each percentage is calculated within the corresponding row category. For example, 45% of DS children with vitamin D deficiency had hypothyroidism, while only 14.16% of those without vitamin D deficiency had hypothyroidism.

Table 3 - Associations with vitamin D deficiency (n=40).

Variable	True n (%)	False n (%)	*P*-value
Hypothyroidism	18 (36.73%)	22 (10.48%)	<0.001
Acquired hypothyroidism	8 (57.14%)	32 (13.06%)	<0.001
Developmental delay	8 (44.44%)	32 (13.28%)	0.002
Intellectual disability	8 (40%)	32 (13.39%)	0.005
Obstructive sleep apnea	4 (57.14%)	36 (14.29%)	0.012
IgA deficiency	2 (100%)	38 (14.79%)	0.023

The percentages in the table represent the proportion of down syndrome (DS) children within each condition who have vitamin D deficiency (True) compared to those without deficiency (False). Each percentage is calculated within the corresponding row category. For example, 36.73% of DS children with hypothyroidism had vitamin D deficiency, while only 10.48% of DS children without hypothyroidism had vitamin D deficiency.

Table 4 - Significant variables affecting growth (Z-scores)

Variable	True: Median (interquartile)	False: Median (interquartile)	*P*-value
Weight Z-score			
Obesity, according to body mass index (BMI)	0.75 (-0.5-1.5)	-1 (-2.0-0.0)	<0.001
Subclinical hypothyroidism	0 (-1.5-0.625)	-1 (-2.0-0.0)	0.027
Acquired hypothyroidism	0.25 (-0.375-1.0)	-1 (-2.0-0.0)	0.004
All hypothyroidism	0 (-1.0-1.0)	-1 (-2.0-0.0)	<0.001
Vitamin D deficiency	0 (-1.0-0.5)	-1 (-2.0-0.0)	<0.001
Obstructive sleep apnea	0 (0.0-0.5)	-1 (-2.0-0.0)	0.011
Congenital heart defects	-1.5 (-2.0-0.0)	-0.5 (-2.0-0.0)	0.022
Height Z-score			
Obesity according to BMI	-2 (-2.0--1.38)	-1.5 (-2.0-0.0)	<0.001
BMI Z-score			
Obesity according to BMI	2 (2.0-2.0)	0 (-2.0-0.5)	<0.001
Subclinical hypothyroidism	1 (-0.125-2.0)	0 (-1.5-1.0)	0.002
Acquired hypothyroidism	1.5 (1.0-1.5)	0 (-1.5-1.0)	0.004
All hypothyroidism	1 (0.0-1.5)	0 (-2.0-1.0)	<0.001
Vitamin D deficiency	0.5 (0.0-1.5)	0 (-2.0-1.0)	<0.001
Obstructive sleep apnea	1 (0.75-1.5)	0 (-1.5-1.0)	0.016
Gastrointestinal structural abnormalities	-1.5 (-2.0-0.0)	0 (-1.5-1.0)	0.039
Family history of endocrinopathies	1.5 (0.75-2.0)	0 (-1.5-1.0)	0.036

because of incomplete data or the unavailability of specific tests at the center, as indicated in Tables 1 and 4.

Obstructive sleep apnea. Obstructive sleep apnea was diagnosed in 2.7% of the study population, with a strong association to obesity in children with DS. OSA was also linked to an increased likelihood of recurrent respiratory infections, which can exacerbate developmental delays (p=0.002). Table 3 presents a detailed overview of the associations mentioned.

Discussion. The findings of this study underscore the significant prevalence of endocrinopathies in children with DS and highlight the considerable impact of these conditions on growth and overall health. These results align with those of previous research, which has demonstrated that hypothyroidism, vitamin D deficiency, and obesity associated with obstructive sleep apnea are the most common endocrinopathies observed in children with DS.

Prevalence and impact of thyroid dysfunction. This study, consistent with other national and international studies, reaffirms that endocrinopathies are prevalent among individuals with DS, with thyroid dysfunction being one of the most frequent endocrine disorders. The rate of thyroid dysfunction in people with Down syndrome varies between 13% and 63%, including issues like subclinical hypothyroidism, congenital hypothyroidism, and autoimmune thyroid disorders such as Graves' disease and Hashimoto's thyroiditis.[10–12] The risk of thyroid dysfunction in individuals with DS is substantially higher than that in the general population.[10-12]

Individuals with DS have a higher likelihood of experiencing other health issues associated with hypothyroidism, such as pericardial effusion, highlighting the need for vigilant monitoring and proactive management of endocrine health in this population.[13] Additionally, patients with DS exhibit a strong predisposition to autoimmune diseases, such as type 1 diabetes mellitus, further emphasizing the complex endocrinopathies they may face.[12,14]

This study also demonstrated an association between congenital hypothyroidism and family history, which is consistent with other research findings. Parental consanguinity has been recognized as an important factor contributing to the prevalence of hypothyroidism in pediatric age group.[15,16] In children with DS, family history of hypothyroidism may increase the risk of congenital hypothyroidism by up to 8-fold.[16] These findings suggest that screening at birth and consistent monitoring are critical in high-risk groups.

In addition, significant associations emerged between hypothyroidism, dyslipidemia, and obesity in individuals with DS. This relationship underlines the importance of understanding complex metabolic risks in this population. Previous studies have indicated that hypothyroidism in obese children had a correlation with insulin resistance, hyperglycemia, dyslipidemia, and increased cardiovascular risk.[17] Moreover, physiological factors, including hypothyroidism, lower

basal metabolic rates, and suboptimal dietary habits, contribute to the predisposition of children with DS toward obesity.[18]

The interplay between hypothyroidism and dyslipidemia in children with DS is complex. Some studies have identified a correlation between leptin and adiponectin levels with obesity in children with hypothyroidism.[19] In contrast, other studies found no significant associations between lipid profiles and thyroid function.[20] Nevertheless, thyroid dysfunction, including subclinical hypothyroidism, has been linked to various metabolic parameters in obese children, reinforcing the need for integrated management of these conditions.[17]

Understanding these relationships is crucial for healthcare providers and researchers, because it emphasizes the necessity of comprehensive monitoring and management of thyroid function, lipid profiles, and weight in patients with DS. This approach could facilitate targeted interventions to mitigate health risks and enhance outcomes in children with DS.

Vitamin D deficiency. In this study, vitamin D deficiency emerged as a prevalent and impactful condition in the DS cohort and was significantly associated with intellectual disability, developmental delay, and IgA deficiency. This finding is critical, as hypovitaminosis D has been linked to musculoskeletal health issues and slow bone mass development. The widespread occurrence of vitamin D deficiency among individuals with DS may be attributed to inadequate sun exposure, insufficient dietary intake, malabsorption issues, and the use of anticonvulsants, which are common in this population.[21–23] As demonstrated in this study, vitamin D deficiency has been linked with various conditions, including immune disorders and metabolic syndrome, including hypothyroidism, all of which can impact the overall health and well-being of individuals with DS.[23–25]

The effects of vitamin D deficiency on DS extend across various domains of health. Individuals with DS have a heightened susceptibility to autoimmune conditions like celiac disease, which is partly attributable to the elevated occurrence of immune-related disorders in this population.[10,12,14] Celiac disease, with associated malabsorption and vitamin deficiencies, is common in patients with DS and has a geographically variable prevalence rate. For instance, celiac disease occurs in 6.7% of children with DS in the Olmsted County compared to 2.6% to 10.3% in the United States and 5% to 8% in the Netherlands.[26]

Celiac disease, characterized by gluten intolerance, can lead to fat malabsorption and vitamin D deficiency. It is especially frequent among individuals with DS, with a prevalence rate ranging from 4% to 15%.[27] Therefore, screening for celiac disease is critical to prevent diagnostic delays and related morbidities in DS.[28]

Vitamin D deficiency can further increase the risk of metabolic syndrome, particularly in obese individuals, and is linked to markers such as hypertriglyceridemia.[29,30] Consistent with other studies, our findings underscore the link between vitamin D deficiency and hypothyroidism, where lower vitamin D levels are correlated with a higher incidence of hypothyroidism and higher levels of thyroid stimulating hormone.[25,31] Vitamin D deficiency has also been linked to clinical manifestations such as seizures, respiratory infections, and abnormal bone development.[22,32,33]

Addressing vitamin D insufficiency in DS is essential for reducing associated health risks. Routine screening for celiac disease, maintaining sufficient vitamin D levels, and exploring vitamin D supplementation—especially for those at higher risk—are essential approaches to improving the health and overall welfare of individuals with DS.

Growth retardation and endocrinopathies. This study confirmed that growth retardation is a prevalent issue in patients with DS, with significant impact on height and a slightly greater effect observed in females compared with males. This is consistent with current studies, indicating that growth retardation in individuals with DS may stem from a lack of growth hormone (GH) resulting from dysfunction in the hypothalamus.[34] This growth impairment was slightly more pronounced in females than in males.

Growth retardation and short stature are key indicators of DS, with approximately 10% of patients presenting with GH deficiency.[35] Studies have demonstrated that individuals with DS exhibit notable growth retardation, which is likely linked to a diminished serum GH response in stimulation tests.[35] Such growth retardation can affect skeletal maturation and result in short stature, affecting overall development.[35]

Studies have explored the hypothesis that GH deficiency in DS is attributable to hypothalamic dysfunction.[34] Additionally, investigations of the pituitary response to GHrH have provided insights into the endocrine mechanisms underlying growth patterns in individuals with genetic syndromes.

Implications for clinical practice. The results of this research highlight the significance of dedicated DS clinics for the prompt identification and treatment of endocrinopathies. for enhancing the health outcomes and quality of life for children with Down syndrome.

Such clinics enable adherence to healthcare guidelines and timely diagnoses, thereby preventing comorbidities and complications associated with untreated endocrinopathies.

The comprehensive care model outlined by the AAP emphasizes a multidisciplinary approach.[36] Pediatricians play a pivotal role in addressing the complex medical needs of children with DS, including screening for common comorbidities such as thyroid disease, celiac disease, and autoimmune conditions. This holistic care approach ensures the prompt identification and management of all potential health issues, thereby enhancing the overall well-being of patients with DS.

Moreover, a national DS care program could significantly improve healthcare delivery by standardizing care protocols and providing essential resources for families and healthcare providers. Multidisciplinary teams, including endocrinologists, cardiologists, and neurologists, are better equipped to address the diverse health needs of patients with DS. Moreover, family education and support are vital, because well-informed families are better equipped to manage the health and developmental challenges associated with DS effectively.

Study limitations. This research presented various limitations. The limited sample size and the single-center approach restrict the applicability of our results to a broader DS population. Additionally, data constraints, such as incomplete documentation and the unavailability of certain diagnostic tests at the study center, restricted the comprehensive evaluation of some DS associated health aspects.

This study highlights the notably increased frequency of endocrinopathies in individuals with DS, underscoring their elevated vulnerability to autoimmune conditions. Hypothyroidism, obesity, type I diabetes mellitus, and OSA emerged as significant comorbidities associated with patients with DS, each having different impacts on growth and development. The significant association of vitamin D deficiency with intellectual disability and developmental delay highlights the importance of systematic screening and timely intervention in populations with DS.

In alignment with international guidelines, implementing national support programs and fostering multidisciplinary care teams can substantially improve the quality of life of individuals with DS. These findings emphasize the necessity of proactive and comprehensive management approaches, and suggest that future research should prioritize optimizing screening protocols and treatment strategies to enhance long-term health results for children with DS.

Acknowledgment. *The authors gratefully acknowledge the Qatif Central Hospital for providing access to medical records and supporting this research. We express our appreciation to the patients and their families, as their data enabled this study to be conducted, and to the Pediatric Department staff for their assistance in data collection and patient follow-up. Special thanks are also due to the hospital's Research and Institutional Review Board for their guidance and to colleagues who provided valuable feedback to improve this work. We extend our gratitude to Editage (www.editage.com) for their assistance with English language editing.*

References

1. Niazi MA, al-Mazyad AS, al-Husain MA, al-Mofada SM, al-Zamil FA, Khashoggi TY. Down's syndrome in Saudi Arabia: incidence and cytogenetics. ***Hum Hered*** 1995; 45: 65-69.
2. Al Hussain M. Growth charts for children with Down's syndrome in Saudi Arabia: birth to 5 years. ***Int J Clin Pr*** 2003; 57: 170-174.
3. M AH. Body mass index for Saudi children with Down's syndrome. ***Acta Paediatr*** 2003; 92: 1482–1485.
4. Fructuoso M, Rachdi L, Philippe E, Denis RG, Magnan C, Le Stunff H. Increased levels of inflammatory plasma markers and obesity risk in a mouse model of Down syndrome. ***Free Radic Biol Med*** 2018: 114: 122-130.
5. Pellegrini FP, Marinoni M, Frangione V, Tedeschi A, Gandini V, Ciglia F. Down syndrome, autoimmunity and T regulatory cells. ***Clin Exp Immunol*** 2012; 169: 238-243.
6. Aitken RJ, Mehers KL, Williams AJ, Brown J, Bingley PJ, Howell RW. Early-onset, coexisting autoimmunity and decreased HLA-mediated susceptibility are the characteristics of diabetes in Down syndrome. ***Diabetes Care*** 2013; 36: 1181-1185.
7. Aversa T, Valenzise M, Corrias A, Salerno M, Iughetti L, Tessaris D. In children with autoimmune thyroid diseases the association with Down syndrome can modify the clustering of extra-thyroidal autoimmune disorders. ***J Pediatr Endocrinol Metab*** 2016; 29: 1041-1046.
8. Lavigne J, Sharr C, Elsharkawi I, Ozonoff A, Baumer N, Brasington C. Thyroid dysfunction in patients with Down syndrome: results from a multi-institutional registry study. ***Am J Med Genet A*** 2017; 173: 1539-1545.
9. Feldman PM, Rodriguez N, Morrison E, Barton B, Lee MM. Prospective study of thyroid function in the first year of life in infants with Down syndrome. ***Eur J Pediatr*** 2023; 182: 2903–2911.
10. Zabeen F, Mohsin F, Jesmin E, Mahbuba S, Hassan MQ. Comorbidities in children with Down syndrome: experience in a tertiary care hospital of Bangladesh. ***Birdem Med J*** 2021; 11: 191–196.
11. Siddiqui M, Iqbal W, Rana M, Sufiyan M, Saleem F, Pervaiz R. Assessment of thyroid hormone abnormalities in patients of Down syndrome. ***Pak J Intens Care Med*** 2022; 2022.
12. Whooten R, Schmitt J, Schwartz A. Endocrine manifestations of Down syndrome. ***Curr Opin Endocrinol Diabetes Obes*** 2018; 25: 61–66.
13. Iqbal R, Wilson JA, Linn HN, Bajwa AT, Devi K, Devarakonda PK. Cardiac tamponade in Down's syndrome associated with hypothyroidism: an uncommon presentation. ***Cureus*** 2024; 16: e59023.

14. Ferrari M, Stagi S. Autoimmunity and genetic syndromes: A focus on Down syndrome. ***Genes (Basel)*** 2021; 12: 268.
15. Heidarpour M, Omoomi S, Vakilbashi O, Taki A, Hovsepian S. Hypothyroidism in first-degree relatives of neonates with congenital hypothyroidism: is there an association? ***Int J Prev Med*** 2023; 14: 109.
16. Corona-Rivera JR, Andrade-Romo TO, Aguirre-Salas LM, Bobadilla-Morales L, Aranda-Sánchez CI, Corona-Rivera A, et al. Family history of thyroid disease and risk of congenital hypothyroidism in neonates with Down síndrome. ***Gac Med Mex*** 2021; 157: 133-139.
17. Kara O. Influence of subclinical hypothyroidism on metabolic parameters in obese children and adolescents. ***Clin Exp Pediatr*** 2020; 63: 110–114.
18. O' Shea M, O' Shea C, Gibson L, Leo J, Carty C. The prevalence of obesity in children and young people with Down syndrome. ***J Appl Res Intellect Disabil*** 2018; 3: 1225–1229.
19. El Amrousy D, El-Afify D, Salah S. Insulin resistance, leptin and adiponectin in lean and hypothyroid children and adolescents with obesity. ***BMC Pediatr*** 2022; 22: 245.
20. Ahmad IH, Elwahab MA, El Wakeel ME, Kamal MA, Elhady M. Oxidative DNA damage and subclinical hypothyroidism in children with obesity. ***Egypt Pediatr Assoc Gaz*** 2021; 69: 15.
21. Stagi S, Lapi E, Romano S, Bargiacchi S, Brambilla A, Giglio S. Determinants of vitamin d levels in children and adolescents with down syndrome. ***Int J Endocrinol*** 2015; 2015: 896758.
22. Altuna M, Giménez S, Fortea J. Epilepsy in Down syndrome: A highly prevalent comorbidity. ***J Clin Med*** 2021; 10: 2776.
23. Pathania M, Dhar M, Kumar A, Saha S, Malhotra R. Association of vitamin D status with metabolic syndrome and its individual risk factors: A cross-sectional study. ***Cureus*** 2023; 15: e38344.
24. Claudia, Rednic S, Grama A, Pop TL. An Update on the effects of vitamin d on the immune system and autoimmune diseases. ***Int J Mol Sci*** 2022; 23: 9784.
25. Ashok T, Palyam V, Azam AT, Odeyinka O, Alhashimi R, Thoota S. Relationship between vitamin D and thyroid: an enigma. ***Cureus*** 2022; 14: e21069.
26. Ostermaier KK, Weaver AL, Myers SM, Stoeckel RE, Katusic SK, Voigt RG. Incidence of Celiac Disease in Down syndrome: A longitudinal, population-based birth cohort Study. ***Clin Pediatr (Phila)*** 2020; 59: 1086–1091.
27. AlRuwaily F, Kattan HA, AlMehaidib AM, AlDekhail W. Prevalence of celiac disease in Saudi children with Down syndrome: A retrospective study. ***Int J Pediatr Adolesc Med*** 2017;4: 51–53.
28. Liu E, Wolter-Warmerdam K, Marmolejo J, Daniels D, Prince G, Hickey F. Routine Screening for Celiac Disease in Children With Down Syndrome Improves Case Finding. ***J Pediatr Gastroenterol Nutr*** 2020; 71: 252–256.
29. Mirhoseini M, Daemi H, Masoom Babaiee M, Asadi-Samani M, Mirhoseini L, Sedehi M. The relationship between vitamin D deficiency and metabolic syndrome in obese individuals. ***J Ren Inj Prev*** 2018; 7: 275-279.
30. Hofman-Hutna J, Hutny M, Matusik E, Olszanecka-Glinianowicz M, Matusik P. Vitamin D deficiency in obese children is associated with some metabolic syndrome components, but not with metabolic syndrome itself. ***Metabolites*** 2023;13: 914.
31. Milyani A. Autoimmunity and Vitamin D Deficiency in Children Affected with Trisomy 21. V A 2018; 22: 3.
32. Begum S, Shyamaly KJ, Tithi BB, Ahkter RO, Parvin R, Karim MR. Management of vitamin D deficiency in children: an update. ***Bangladesh J Child Health*** 2019; 73.
33. Santoro SL, Chicoine B, Jasien JM, Kim JL, Stephens M, Bulova P, et al. Pneumonia and respiratory infections in Down syndrome: A scoping review of the literature. ***Am J Med Genet A*** 2021; 185: 286–299.
34. Metwalley KA, Farghaly HS. Endocrinal dysfunction in children with Down syndrome. ***Ann Pediatr Endocrinol Metab*** 2022; 27: 15–21.
35. Meguri K, Inoue M, Narahara K, Sato T, Takata A, Ohki N. Therapeutic efficacy and safety of GH in Japanese children with Down syndrome short stature accompanied by GH deficiency. ***Clin Pediatr Endocrinol*** 2013; 22: 65–72.
36. Bull MJ, Trotter T, Santoro SL, Christensen C, Grout RW, Burke LW. Health supervision for children and adolescents with Down syndrome. ***Pediatrics*** 2022; 149: e2022057010.