REABILITACIJOS MOKSLAI
Slauga, kineziterapija, ergoterapija
LSU LITHUANIAN SPORTS UNIVERSITY

Reabilitacijos mokslai: slauga, kineziterapija, ergoterapija, *1*(34) 2026, 147–158, eISSN 2538-8673; DOI: https://doi.org/10.33607/rmske.v1i34.2277

Association Between Serum 25-Hydroxyvitamin D Levels and Gross Motor Development in Children With Down Syndrome: An Analytical Cross-Sectional Study

Esmire Tërshnjaku Sadiku[1], Lence Aleksovska Velickovska[2], Samire Beqaj[3], Mejdi Aliu[3, 4]*

[1] Down Syndrome Association Kosovo, Prishtina, Kosovo
[2] Faculty of Physical Education, Sport and Health, Cyril and Methodius University in Skopje, Skopje, North Macedonia
[3] Department of Physiotherapy, Faculty of Medicine, University of Prishtina, Prishtina, Kosovo
[4] Department of Physiotherapy, Faculty of ECM, Alma Mater Europaea University, Maribor, Slovenia
* Correspondence: mejdi.aliu@almamater.si

Abstract

Background. Down syndrome (DS) is associated with delayed gross motor development, and vitamin D deficiency is frequently reported in this population. However, evidence regarding the relationship between vitamin D status and motor development in children with DS is limited.

Aim. To examine the association between serum 25-hydroxyvitamin D [25(OH)D] levels and gross motor development in children with DS.

Methods. This analytical cross-sectional study included 33 children with DS (13 females and 20 males) aged 1.00–6.56 years (mean age 2.53 ± 1.06 years). Gross motor development was assessed using the Basic Motor Skills (BMS) Test. Serum 25(OH)D concentrations were measured using electrochemiluminescence on a Cobas® e 411 analyser (*Roche Diagnostics*). Vitamin D status was categorised as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Associations between vitamin D levels and gross motor milestones were evaluated using Spearman's rank correlation and group comparisons.

Results. Vitamin D deficiency was observed in 36.4% of the participants, 12.1% had insufficient vitamin D levels, and 51.5% had sufficient vitamin D levels. No statistically significant correlations were found between serum 25(OH)D levels and any gross motor milestone (r range −0.172 to 0.292; all $p > 0.05$). The strongest correlation was observed for adopting a sitting position ($r = 0.292$), but it was not statistically significant ($p = 0.099$).

Conclusions. Vitamin D deficiency appears to be common in children with DS, while no significant association was observed between serum 25(OH)D levels and gross motor development in this sample. These findings highlight the need for larger, longitudinal studies to further clarify this relationship.

Keywords: Down syndrome; 25-hydroxyvitamin D; vitamin D deficiency; gross motor development; children

1. INTRODUCTION

Down syndrome (DS), known as trisomy 21 in genetic terms, is a prevalent chromosomal anomaly occurring at a frequency of approximately 1 in 400 to 1 in 1,500 live births worldwide. Individuals with DS possess an extra copy of chromosome 21, resulting in substantial modifications in both physical and cognitive development. The syndrome manifests in three primary forms: trisomy, translocation, and mosaicism. The phenotype associated with DS encompasses a range of clinical features that impact various physiological systems, notably the musculoskeletal, neurological, and cardiovascular (Antonarakis et al., 2020; Kazemi et al., 2016; Rodríguez-Grande et al., 2021; Shin et al., 2010; Shields, 2021).

Motor development in children with DS is markedly delayed compared with that of typically developing peers, with gross motor milestones such as reaching, sitting, crawling, and walking often achieved at nearly twice the expected age (Beqaj et al., 2017; Jain et al., 2021; Lauteslager, 2004). These motor impairments are likely influenced by multiple physiological and developmental factors, among which vitamin D has attracted increasing attention because of its established role in musculoskeletal health. In addition to its skeletal effects, vitamin D may contribute to functional mobility and reduced fall risk by supporting muscle function and addressing metabolic and musculoskeletal abnormalities in individuals with DS. Vitamin D deficiency is frequently reported in children with DS. The underlying factors contributing to this deficiency in DS children include muscular hypotonia, sedentary lifestyle, inadequate dietary intake, hypogonadism, stunted growth, and thyroid dysfunction. Furthermore, certain exacerbating factors like obesity and a history of autoimmune disorders have been identified (Bokhari et al., 2018; Büyükavcı & Büyükavcı, 2021; Stagi et al., 2015; Valle et al., 2025).

Despite the high prevalence of vitamin D deficiency and motor delay in children with DS, an important research gap remains regarding the association between vitamin D status and gross motor development. The existing evidence on the relationship between vitamin D and motor outcomes is still inconclusive. Existing evidence is largely derived from studies conducted in general paediatric populations using diverse approaches to the assessment of vitamin D status and motor outcomes. Moreover, studies involving children with developmental disabilities are scarce, and evidence specifically focusing on children with DS is notably lacking. The lack of empirical studies, unclear underlying mechanisms, unexamined supplementation strategies, and absence of longitudinal investigations present specific areas for future research. Conducting a well-structured cross-sectional study could greatly enhance the comprehension of the factors influencing motor development in individuals with DS and potentially unveil a modifiable risk element that could be promptly applied in clinical settings. Therefore, the principal aim of this cross-sectional investigation was to explore the correlation between various vitamin D levels and the attainment of gross motor milestones in children with DS.

2. METHODS

2.1. Study design and participants

This study utilised an analytical cross-sectional methodology to investigate the correlation between serum vitamin D levels and the development of gross motor skills in children with DS (Capili, 2021). The reporting of the study followed the recommendations of the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies (von Elm et al., 2007).

In total, 33 children diagnosed with DS were enrolled in the study, comprising 13 females (39.4%) and 20 males (60.6%). At the time of evaluation, the average age of the participants was 2.53 ± 1.06

years (equivalent to 30.4 ± 12.7 months), with ages ranging from 1.00–6.56 years. The demographic attributes of the participants are presented in Table 1.

The rationale for selecting this specific cohort stemmed from the heightened susceptibility of children with DS to vitamin D insufficiency and delays in gross motor skill development, rendering this population pertinent for exploring potential connections between vitamin D status and motor developmental outcomes.

Table 1. **Participant characteristics**

Characteristic	Value
Sample size (*N*)	33
Sex – Female, *n* (%)	13 (39.4%)
Sex – Male, *n* (%)	20 (60.6%)
Age at sampling (mean ± SD), years	2.53 ± 1.06
Age at sampling (mean ± SD), months	30.4 ± 12.7
Age range, years (months)	1.00–6.56

Notes: n – number; % – percentage; SD – standard deviation.

2.2. Ethical approval and informed consent

This research adhered to the ethical guidelines outlined in the Declaration of Helsinki (World Medical Association, 2013) and the approval for the research was obtained from the Ethics Council of the Physiotherapists' Chamber of Kosovo under protocol No. 588, PKE/42. Before inclusion in the study, parents or legal guardians were provided with a comprehensive overview of the research objectives and methodologies. Subsequently, written consent was obtained from all parents or legal guardians. The data were de-identified and treated with confidentiality in accordance with ethical guidelines.

2.3. Sampling and recruitment procedures

Children were eligible for inclusion if they had a genetically confirmed diagnosis of DS, were registered members of the Down Syndrome Association Kosovo (DSK), were receiving physiotherapy treatment, had parents/legal guardians who provided written informed consent, and were aged 1–6 years. Children were excluded if they had major medical conditions, such as significant cardiac disease or uncontrolled seizures.

A convenience sampling technique was used to identify and approach 39 eligible participants. All parental figures or legal guardians provided consent for involvement, yielding an 85% response rate in this study. There were no exclusions post-enrolment, and the dataset remained free from any instances of missing or incomplete information.

2.4. Outcome measures and instruments

The main focus of the research was gross motor development as the primary outcome, which was evaluated using the Basic Motor Skills (BMS) assessment. The secondary outcome was the measurement of serum 25-hydroxyvitamin D [25(OH)D] levels in nanograms per millilitre, measured using

electrochemiluminescence (ECL). The analysis involved both continuous quantitative evaluation and categorisation into deficient, insufficient, and sufficient vitamin D status groups.

Gross motor development was assessed using the BMS assessment, this test is a validated and reliable clinician-administered instrument specifically developed for children with DS. It has demonstrated satisfactory reliability and validity for assessing gross motor development and postural control in this population and is widely used in clinical settings. The BMS comprises 15 milestones, each corresponding to a specific motor task. In the present study, milestones 7 to 15 were included in the analysis because, given the age profile of the participants (mean age 2.53 ± 1.06 years; range 1.00–6.56 years), the first six milestones were expected to show limited variability and potential ceiling effects. The nine analysed gross motor milestones were as follows: sitting, moving forwards over the ground, walking with support, standing with support, standing up with support, standing without support, adopting a sitting position, walking without support, and standing up without support. Each milestone was scored on a four-level ordinal scale (SC0–SC3), with higher scores indicating greater motor competence. Detailed scoring rules and milestone subdivisions were assessed according to the BMS assessment manual (Lauteslager, 2004; Lauteslager et al., 2020; van den Heuvel et al., 2009).

Serum 25-hydroxyvitamin D [25(OH)D] levels were assessed utilising an ECL technique with the Cobas e 411 analyser from Roche Diagnostics (Wielders et al., 2014). The children were categorised into three groups based on their serum 25-hydroxyvitamin D [25(OH)D] levels as follows: deficient (<20 ng/mL), insufficient (20–29 ng/mL), and sufficient (≥30 ng/mL) (Holick, 2009).

2.5. Data collection procedures

The study was conducted at DSK centres in Prishtina, Prizren, and Ferizaj. The primary method of data collection involved informing parents or legal guardians about the study's objectives and procedures by the principal investigator. Subsequent to a comprehensive explanation of the study, formal written consent was obtained from the parents or legal guardians before their involvement in the research.

The participants underwent two distinct evaluations. Initially, serum vitamin D levels were assessed at a designated clinical laboratory. Standardised laboratory protocols were followed for all paediatric participants under the supervision of competent microbiology experts. Parents or legal guardians accompanied the children to the laboratory for blood sample collection and measurement of serum 25-hydroxyvitamin D [25(OH)D]. The findings were relayed to the principal investigator, who communicated the results to the participants' parents or legal guardians.

Subsequently, the participants' gross motor skills were evaluated by certified paediatric physiotherapists with expertise and training in administering the BMS assessment for children with DS. This evaluation took place at the DSK centres in the presence of parents or legal guardians and lasted approximately 45 minutes.

Three identical hard copies of the vitamin D and detailed BMS assessment were completed: one for the parents or legal guardians, one for the child's records at the DSK centre, and one for electronic data capture by the principal investigator. All data collected were meticulously reviewed for accuracy and transcribed from hard copies to an electronic repository for subsequent analyses.

2.6. Statistical analysis

The statistical analysis was conducted utilising IBM SPSS Statistics software (version 22). Descriptive statistics were employed to present a summary of the data, encompassing means, standard deviations, and ranges for continuous variables, as well as frequencies and percentages for categorical variables. Within-group variances were assessed utilising Fisher's Exact Test for categorical compari-

sons due to the presence of limited expected cell counts in multiple contingency tables. The relationship between serum vitamin D concentrations and gross motor development was scrutinised through Spearman's rank correlation coefficient. Statistical significance was inferred at a p-value below 0.05.

3. RESULTS

3.1. Distribution of serum 25-hydroxyvitamin D [25(OH)D] divided by vitamin D status and sex

Among the children with DS included in the study, 12 (36.4%, 95% CI 22.2–53.4) were classified as vitamin D deficient (<20 ng/mL), four (12.1%, 95% CI 4.8–27.3) as insufficient (20–29 ng/mL), and 17 (51.5%, 95% CI 35.1–67.6) as sufficient (≥30 ng/mL). Confidence intervals were calculated using the Wilson score method (Table 2).

Table 2. **Distribution of serum 25-hydroxyvitamin D [25(OH)D] categories among children with DS**

VD ng/mL	N	%	95% CI (Wilson)
Deficient <20 ng/mL	12	36.4%	22.2% – 53.4%
Insufficient 20–29 ng/mL	4	12.1%	4.8% – 27.3%
Sufficient ≥30 ng/mL	17	51.5%	35.1% – 67.6%
Total	33	100%	

Notes: VD – vitamin D; ng/mL – nanograms per millilitre; N – sample size; CI – confidence interval.

Sex-stratified analysis showed comparable mean serum 25-hydroxyvitamin D [25(OH)D] concentrations in females and males. Females (N = 13) had a mean 25(OH)D of 30.12 ± 16.80 ng/mL (95% CI 19.96–40.27); subgroup means were 15.54 ng/mL (deficient, n = 5), 25.20 ng/mL (insufficient, n = 2), and 43.90 ng/mL (sufficient, n = 6). Males (N = 20) had a mean of 30.90 ± 15.97 ng/mL (95% CI 23.43–38.38); subgroup means were 18.30 ng/mL (deficient, n = 7), 22.27 ng/mL (insufficient, n = 2), and 40.49 ng/mL (sufficient, n = 11). The overall mean for the cohort was 30.59 ± 16.05 ng/mL (min 10.40, max 70.90) (Table 3).

Table 3. **Vitamin D status and subgroup means by sex**

VD ng/mL		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
F	Deficient	5	15.5400	3.48109	1.55679	11.2177	19.8623	10.40	18.90
	Insufficient	2	25.2000	1.97990	1.40000	7.4113	42.9887	23.80	26.60
	Sufficient	6	43.9000	14.73336	6.01487	28.4383	59.3617	30.20	64.20
	Total	13	30.1154	16.80371	4.66051	19.9610	40.2698	10.40	64.20

VD ng/mL		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
M	Deficient	7	18.3029	1.28091	0.48414	17.1182	19.4875	16.92	19.90
	Insufficient	2	22.2650	1.22329	0.86500	11.2741	33.2559	21.40	23.13
	Sufficient	11	40.4945	16.01284	4.82805	29.7370	51.2521	20.10	70.90
	Total	20	30.9045	15.97367	3.57182	23.4286	38.3804	16.92	70.90
Overall		33	30.5936	16.04806	2.79	24.90	36.28	10.40	70.90

Notes: VD – vitamin D; ng/mL – nanograms per millilitre; N – sample size; F – female; M – male; Std. – standard. Classification cutoffs: deficient <20 ng/mL; insufficient 20–29 ng/mL; sufficient ≥30 ng/mL. Assay: ECL on Cobas e 411 (Roche Diagnostics).

According to vitamin D status, the mean 25(OH)D concentrations were 17.15 ± 2.71 ng/mL (deficient, $N = 12$), 23.73 ± 2.16 ng/mL (insufficient, $N = 4$), and 41.70 ± 15.20 ng/mL (sufficient, $N = 17$). The sufficient group exhibited greater variability than the insufficient/deficit groups (Table 4).

Table 4. **Serum 25(OH)D by vitamin D status**

VD ng/mL	N	Minimum	Maximum	Mean	Std. Deviation
Deficient	12	10.40	19.90	17.1517	2.70656
Insufficient	4	21.40	26.60	23.7325	2.16261
Sufficient	17	30.10	70.90	41.6965	15.19559

Notes: VD – vitamin D; ng/mL – nanograms per millilitre; N – sample size. Classification cutoffs: deficient <20 ng/mL; insufficient 20–29 ng/mL; sufficient ≥30 ng/mL. Assay: ECL on Cobas e 411 (Roche Diagnostics).

3.2. Evaluation of the association between gross motor milestones and vitamin D status

To evaluate the relationship between vitamin D status and gross motor function, we compared the proportion of children who completed each milestone (score = 3) in each vitamin D category. No milestones differed significantly according to vitamin D status (all $p > 0.05$). For example, the completion rates for sitting were 66.7% (deficient), 75.0% (insufficient), and 76.5% (sufficient) ($p = 0.956$). Stand without support showed a non-significant trend (8.3% vs. 100.0% vs. 47.1% for deficient, insufficient, sufficient; $p = 0.080$) but did not reach statistical significance (Table 5).

Table 5. **Association between gross motor development milestones (completed = score 3) and vitamin D status**

Milestone	Deficient (*N* = 12) n (%)	Insufficient (*N* = 4) n (%)	Sufficient (*N* = 17) n (%)	P-value
Sitting	8 (66.7%)	3 (75.0%)	13 (76.5%)	0.956
Move forwards over ground	8 (66.7%)	0 (0.0%)	11 (64.7%)	0.655
Walk with support	7 (58.3%)	4 (100.0%)	11 (64.7%)	0.393
Stand with support	9 (75.0%)	4 (100.0%)	11 (64.7%)	0.504
Stand up with support	7 (58.3%)	4 (100.0%)	11 (64.7%)	0.410
Stand without support	1 (8.3%)	4 (100.0%)	8 (47.1%)	0.080
Adopt sitting position	4 (33.3%)	3 (75.0%)	12 (70.6%)	0.318
Walk without support	2 (16.7%)	2 (50.0%)	8 (47.1%)	0.201
Stand up without support	2 (16.7%)	1 (25.0%)	8 (47.1%)	0.272

Notes: N – sample size; n – number; % – percentage. Classification cutoffs: deficient <20 ng/mL; insufficient 20–29 ng/mL; sufficient ≥30 ng/mL. Assay: ECL on Cobas e 411 (Roche Diagnostics).

Spearman's rho correlation analysis ($N = 33$) between continuous serum 25(OH)D (ng/mL) and each gross motor milestone (ordinal 0–3) did not reveal any statistically significant associations (r range −0.172 to 0.292; all $p > 0.05$). The largest observed correlation coefficient ($r = 0.292$ for "adopt sitting position") was not statistically significant ($p = 0.099$) (Table 6).

Table 6. **Spearman's rho correlations between serum 25(OH)D (ng/mL) and gross motor milestones**

Variable	Sitting	Move forwards over the ground	Walk with support	Stand with support	Stand up with support	Stand without support	Adopt sitting position	Walk without support	Stand up without support
Correlation coefficient (r)	–0.005	–0.164	–0.064	–0.172	–0.003	0.133	0.292	0.007	0.080
p-value	0.980	0.362	0.725	0.338	0.985	0.460	0.099	0.968	0.659

4. DISCUSSION

This analytical cross-sectional study provides novel evidence on the relationship between serum 25-hydroxyvitamin D [25(OH)D] and gross motor development in young children with DS. To the best of our knowledge, no published study has specifically examined this association in children with DS. The principal findings indicate that, although vitamin D deficiency and insufficiency were common within the cohort, no statistically significant association was observed between vitamin D status and gross motor development. Additionally, serum 25(OH)D concentrations were comparable between the sexes, and no clear age-related trend was identified, with substantial variability in vitamin D levels across the studied age range.

The prevalence of suboptimal vitamin D levels observed in this study is consistent with previous DS-specific research showing a high burden of vitamin D deficiency among children with DS. Büyükavcı and Büyükavcı (2021) reported a deficiency rate of 75% in preschool children with DS under six years of age, whereas Bokhari et al. (2018) found a prevalence of 65.5% in children with DS up to 18 years of age. In our investigation, the prevalence was lower at 36.6% in children with DS older than six years, suggesting variability in vitamin D status across age groups and study populations. However, reported prevalence rates vary considerably across studies, likely due to heterogeneity in age groups, geographic exposure to sunlight, nutritional habits, supplementation practices, and methodological differences in defining deficiency thresholds.

Regarding age-related patterns, Büyükavcı and Büyükavcı (2021) reported a gradual decline in vitamin D levels from infancy through toddlerhood and preschool age in children with DS, whereas Boyd et al. (2023) observed that advanced age corresponded to increased vitamin D levels in individuals with DS. In our cohort, serum 25(OH)D concentrations did not show a clear age-related pattern, and values varied considerably across age groups. Also, vitamin D concentrations demonstrated marked inter-individual variability, indicating that age may not be a reliable determinant of vitamin D status in this population.

Similarly, no statistically significant sex difference was observed, which is consistent with the findings of Boyd et al. (2023). These findings further support the notion that biological sex may not play a major role in determining vitamin D status in individuals with DS.

With regard to the association between vitamin D and motor development, the current findings contribute to an ongoing and inconclusive body of evidence. While some studies in general paediatric populations have suggested that lower vitamin D levels may be linked to delayed motor or neurodevelopmental outcomes, others have failed to confirm such associations (Supriadi et al., 2022; Tavakolizadeh et al., 2019; Zhang et al., 2023). Similarly, intervention-based and longitudinal studies have produced inconsistent results, with some indicating benefits of vitamin D supplementation on developmental milestones, whereas others report minimal or no effect on motor outcomes (Mutua et al., 2020; Praticò et al., 2024; Rodgers al., 2023; Weiler et al., 2022; Wicklow et al., 2015). However, studies in the general paediatric population are less directly applicable to our research question. The present study is particularly important because DS-specific evidence, as well as evidence in children with developmental delays more broadly, remains scarce. Our findings suggest that gross motor development in children with DS may be influenced more strongly by condition-specific factors such as hypotonia, ligamentous laxity, and neurodevelopmental delay than by vitamin D status alone.

From a clinical perspective, although no direct association with motor outcomes was identified, the relatively high proportion of children with suboptimal vitamin D levels underscores the importance of routine screening and appropriate management of vitamin D deficiency in children with DS. Given the established extra-skeletal roles of vitamin D, including its involvement in immune regulation, muscle

function, and metabolic processes, maintaining adequate levels remains clinically relevant, particularly in populations at increased risk of deficiency (Arizmendi et al., 2020; Stagi et al., 2015). It is therefore recommended that individuals with DS undergo assessment of serum 25(OH)D levels and receive appropriate vitamin D supplementation when deficiency is present, especially in those with additional health conditions such as obesity and autoimmune diseases (Arizmendi et al., 2020; Boyd et al., 2023; Eid et al., 2022; Stagi et al., 2015).

Several limitations should be acknowledged when interpreting these findings. First, the cross-sectional design precludes any inference of causality between vitamin D status and motor development. Second, the relatively small sample size and the use of a convenience sampling approach may limit the generalisability of the results and reduce statistical power to detect subtle associations. Third, potential confounding variables, genetical type of DS, sun exposure, dietary intake, vitamin D supplementation, physical activity, seasonal variation, and comorbid conditions, were not systematically controlled. Additionally, the assessment of motor development, although conducted using a structured and validated tool, may still be influenced by evaluator-related variability and the inherent heterogeneity of motor development in children with DS.

5. CONCLUSIONS AND PERSPECTIVES

This analytical cross-sectional study demonstrated that vitamin D deficiency and insufficiency are prevalent in young children with DS. However, in our sample, no statistically significant association was found between serum 25-hydroxyvitamin D [25(OH)D] levels and gross motor development; therefore, these findings should be interpreted with caution due to the limited sample size, design constraints, and lack of control for potential confounders.

Future research should prioritise longitudinal designs to better elucidate the temporal relationship between vitamin D status and motor development. Larger, multicentre studies with stratification by age, sex, and clinical characteristics are warranted. Furthermore, randomised controlled trials examining the effect of vitamin D supplementation on motor outcomes in children with DS would provide more definitive evidence. Incorporating detailed assessments of environmental and lifestyle factors, as well as repeated biochemical measurements, would also enhance the understanding of determinants of vitamin D status in this population.

Author Contributions: Conceptualisation, L.A.V. and E.T.S.; methodology, L.A.V. and E.T.S.; software, E.T.S.; validation, E.T.S., and S.B.; formal analysis, M.A.; investigation, E.T.S.; resources, E.T.S.; data curation, M.A.; writing—original draft preparation, M.A.; writing—review and editing, M.A. and S.B.; visualisation, M.A.; supervision, L.A.V. and S.B.; project administration, E.T.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Acknowledgements: We express our appreciation to the staff of the Down Syndrome Association Kosovo, along with the children and parents.

Conflicts of Interest: The authors declare no conflict of interest.

References

Antonarakis, S. E., Skotko, B. G., Rafii, M. S., Strydom, A., Pape, S. E., Bianchi, D. W., Sherman, S. L., & Reeves, R. H. (2020). Down syndrome. *Nature Reviews Disease Primers*, *6*, 9. https://doi.org/10.1038/s41572-019-0143-7

Arizmendi, K. A. F., Tapia, Y. Y. G., Velazquez, F. J. M., Robledo, T. T. V., Hernandez, L. E. C., & de la Puente, S. G. (2020). Additional health care recommendations for children with Down syndrome. *Journal of Pediatrics & Neonatal Care*, *10*(5), 148–154. https://doi.org/10.15406/jpnc.2020.10.00428

Beqaj, S., Jusaj, N., & Živković, V. (2017). Attainment of gross motor milestones in children with Down syndrome in Kosovo – Developmental perspective. *Medicinski Glasnik*, *14*(2), 189–198. https://doi.org/10.17392/917-17

Bokhari, M. O., Mujallid, M. F., Alsulami, S. A., Milyani, A. A., Alsulami, M. A., Malatani, N. N., Al-Sharief, R. A., Alsolami, M. A., & Al-Agha, A. E. (2018). Autoimmunity and vitamin D deficiency in children affected with trisomy 21. *Current Pediatric Research*, *22*(3).

Boyd, N. K., Nguyen, J., Khoshnood, M. M., Jiang, T., Nguyen, L., Mendez, L., Spinazzi, N. A., Manning, M. A., Rafii, M. S., & Santoro, J. D. (2023). Hypovitaminosis D in persons with Down syndrome and autism spectrum disorder. *Journal of Neurodevelopmental Disorders*, *15*, 35. https://doi.org/10.1186/s11689-023-09503-y

Büyükavcı, R., & Büyükavcı, M. A. (2021). Vitamin D deficiency in preschool children with Down syndrome. *Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Dergisi*, *16*(3), 397–400. https://doi.org/10.17517/ksutfd.798173

Capili, B. (2021). Cross-sectional studies. *American Journal of Nursing*, *121*(10), 59–62. https://doi.org/10.1097/01.naj.0000794280.73744.fe

Eid, M. A., Ibrahim, M. M., Radwan, N. L., & Aly, S. M. (2022). Effects of vitamin D supplementation and aerobic exercises on balance and physical performance in children with Down syndrome. *International Journal of Therapy and Rehabilitation*, *29*(2), 1–11. https://doi.org/10.12968/ijtr.2020.0162

Holick, M. F. (2009). Vitamin D status: Measurement, interpretation, and clinical application. *Annals of Epidemiology*, *19*(2), 73–78. https://doi.org/10.1016/j.annepidem.2007.12.001

Jain, P. D., Nayak, A., Karnad, S. D., & Doctor, K. N. (2021). Gross motor dysfunction and balance impairments in children and adolescents with Down syndrome: A systematic review. *Clinical and Experimental Pediatrics*, *65*(3), 142–149. https://doi.org/10.3345/cep.2021.00479

Kazemi, M., Salehi, M., & Kheirollahi, M. (2016). Down syndrome: Current status, challenges and future perspectives. *International Journal of Molecular and Cellular Medicine*, *5*(3), 125–133.

Lauteslager, P. E. (2004). *Children with Down's syndrome: Motor development and intervention* [Doctoral dissertation, Heeren Loo Zorggroep].

Lauteslager, P. E. M., Volman, J. M., Lauteslager, T., Van den Heuvel, M. E., Jongerling, J., & Klugkist, I. G. (2020). Basic motor skills of children with Down syndrome: Creating a motor growth curve. *Pediatric Physical Therapy*, *32*(4), 375–380. https://doi.org/10.1097/pep.0000000000000743

Mutua, A. M., Nampijja, M., Elliott, A. M., Pettifor, J. M., Williams, T. N., Abubakar, A., Webb, E. L., & Atkinson, S. H. (2020). Vitamin D status is not associated with cognitive or motor function in pre-school Ugandan children. *Nutrients*, *12*(6), 1662. https://doi.org/10.3390/nu12061662

Praticò, A. D., Lo Bianco, M., Leonardi, R., Polizzi, A., & Ruggieri, M. (2024). The impact of vitamin D supplementation duration on early childhood developmental milestones: A retrospective study. *Nutrients*, *16*(24), 4395. https://doi.org/10.3390/nu16244395

Rodgers, M. D., Mead, M. J., McWhorter, C. A., Ebeling, M. D., Shary, J. R., Newton, D. A., Baatz, J. E., Gregoski, M. J., Hollis, B. W., & Wagner, C. L. (2023). Vitamin D and child neurodevelopment—A post hoc analysis. *Nutrients*, *15*(19), 4250. https://doi.org/10.3390/nu15194250

Rodríguez-Grande, E.-I., Buitrago-Lopez, A., Torres-Narvaez, M.-R., Serrano-Villar, Y., Verdugo-Paiva, F., & Ávila, C. (2021). Therapeutic exercise to improve motor function among children with Down syndrome aged 0 to 3 years: A systematic literature review. *Research Square.* Advance online publication. https://doi.org/10.21203/rs.3.rs-1080112/v1

Shields, N. (2021). Physiotherapy management of Down syndrome. *Journal of Physiotherapy*, *67*(4), 243–251. https://doi.org/10.1016/j.jphys.2021.08.016

Shin, M., Siffel, C., & Correa, A. (2010). Survival of children with mosaic Down syndrome. *American Journal of Medical Genetics Part A*, *152A*(3), 800–801. https://doi.org/10.1002/ajmg.a.33295

Stagi, S., Lapi, E., Romano, S., Bargiacchi, S., Brambilla, A., Giglio, S., Seminara, S., & de Martino, M. (2015). Determinants of vitamin D levels in children and adolescents with Down syndrome. *International Journal of Endocrinology*, *2015*, 1–11. https://doi.org/10.1155/2015/896758

Supriadi, S., Setiabudi, D., Noviandhari, A., Judistiani, R. T. D., Setiabudiawan, B., & Dhamayanti, M. (2022). Correlation between cord blood vitamin D levels and problem-solving neurodevelopment in early childhood: A cohort study in rural Indonesia. *Children*, *9*(10), 1581. https://doi.org/10.3390/children9101581

Tavakolizadeh, R., Ardalani, M., Shariatpanahi, G., Mojtahedi, S. Y., & Sayarifard, A. (2019). Is there any relationship between vitamin D deficiency and gross motor development in 12-month-old children? *Iranian Journal of Child Neurology*, *13*(3), 55–60.

Valle, M. S., Russo, C., Surdo, S., Cambria, M. T., Campanella, M., Tuttobene, M., & Malaguarnera, L. (2025). Pathophysiological role of Vitamin D deficiency in Down syndrome: Insights into metabolic dysfunction and sarcopenia. *International Journal of Molecular Sciences*, *26*(21), 10756. https://doi.org/10.3390/ijms262110756

van den Heuvel, M. E., de Jong, I., Lauteslager, P. E. M., & Volman, M. J. M. (2009). Responsiveness of the test of basic motor skills of children with Down syndrome. *Physical & Occupational Therapy in Pediatrics*, *29*(1), 71–85. https://doi.org/10.1080/01942630802574890

von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., Vandenbroucke, J. P., & for the STROBE Initiative. (2007). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *PLoS Medicine*, *4*(10), e296. https://doi.org/10.1371/journal.pmed.0040296

Weiler, H. A., Hazell, T. J., Majnemer, A., Vanstone, C. A., Gallo, S., & Rodd, C. J. (2022). Vitamin D supplementation and gross motor development: A 3-year follow-up of a randomized trial. *Early Human Development*, *171*, 105615. https://doi.org/10.1016/j.earlhumdev.2022.105615

Wicklow, B., Gallo, S., Majnemer, A., Vanstone, C., Comeau, K., Jones, G., L'Abbe, M., Khamessan, A., Sharma, A., Weiler, H., & Rodd, C. (2015). Impact of vitamin D supplementation on gross motor development of healthy term infants: A randomized dose-response trial. *Physical & Occupational Therapy in Pediatrics*, *36*(3), 330–342. https://doi.org/10.3109/01942638.2015.1050150

Wielders, J. P. M., Carter, G. F., Eberl, H., Morris, G., Roth, H. J., & Vogl, C. (2014). Automated competitive protein-binding assay for total 25-OH vitamin D, multicenter evaluation and practical performance. *Journal of Clinical Laboratory Analysis*, *29*(6), 451–461. https://doi.org/10.1002/jcla.21793

World Medical Association. (2013). World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. *The Journal of the American Medical Association*, *310*(20), 2191–2194. https://doi.org/10.1001/jama.2013.281053

Zhang, Y., Zhou, C.-Y., Wang, X.-R., Jiao, X.-T., Zhang, J., Tian, Y., Li, L.-L., Chen, C., & Yu, X.-D. (2023). Maternal and neonatal blood vitamin D status and neurodevelopment at 24 months of age: A prospective birth cohort study. *World Journal of Pediatrics*, *19*(9), 883–893. https://doi.org/10.1007/s12519-022-00682-7

Zhu, P., Tong, S.-L., Hao, J.-H., Tao, R.-X., Huang, K., Hu, W.-B., Zhou, Q.-F., Jiang, X.-M., & Tao, F.-B. (2015). Cord blood vitamin D and neurocognitive development are nonlinearly related in toddlers. *Journal of Nutrition*, *145*(6), 1232–1238. https://doi.org/10.3945/jn.114.208801

Received 2026 04 03
Accepted 2026 05 31