Acta Orthop. Belg., 2022, **88**, 217-221

ORIGINAL STUDY

doi.org/ 10.52628/88.2.8784

Is the level of vitamin D deficiency correlated with the severity and bilaterality in slipped capital femoral epiphysis? A case series study

Shady Elbeshry, Tarek Hassan Abdelaziz, Ahmad Saeed Aly, Shady Mahmoud

From Ain Shams University Hospitals, Cairo, Egypt

The aim of the study is to find the correlation between vitamin D level and the severity of slippage and bilateral development in slipped capital femoral epiphysis (SCFE) cases if any. Thirty-nine patients with moderate-severe stable SCFE were evaluated regarding their vitamin D level and to which extent the severity of vitamin D deficiency, if present, can be correlated with the severity and bilaterality of the slip. Vitamin D serum level was assessed pre-operatively for all patients. In case of deficiency, the patient underwent in situ pinning unless performed before his/her presentation. Alongside, he/she received a vitamin D course until correction prior to the definitive surgery (Imhäuser osteotomy with osteochondroplasty) 6-12 weeks after. Thereafter, osteotomy healing and physis closure were monitored radiologically. Results show that all patients but one had vitamin D deficiency, with an average of 14.39 ng/mL, necessitating vitamin D therapy before proceeding to the definitive surgery. No correlation existed between vitamin D level and Southwick angle severity with a p-value of 0.85. A negative correlation existed between vitamin D level and bilaterality, but not statistically significant (p-value 0.192). Patients' osteotomy healing was uneventful, and physeal closure was achieved in all the cases that had in situ pinning. We conclude that the severity of Vitamin D deficiency could be linked to the bilateral development of SCFE but not the severity of slippage. Treatment of Vitamin D deficiency facilitates physeal closure.

INTRODUCTION

SCFE is an adolescent hip disorder in which the femoral neck and shaft displace relative to the femoral epiphysis via the physis. Its incidence is 0.2 - 10 per 100.000 *(1)*. SCFE is classified radiologically based on frog lateral Southwick angle that places the slip into mild (< 30^0), moderate ($30\text{-}50^0$), and severe (>50^0) *(2)*.

The pathogenesis of SCFE is not exactly clear, but it is the result of high loads on normal physis, normal loads on weakened physis, or both *(3)*. High loads on the physis occur in cases of increased body mass index (BMI), femoral retroversion, or increased physeal obliquity *(4)*. Physeal weakness might be at the cellular level of chondrocytes in the hypertrophic layer as a result of dysregulation of different pathways signals that are affected by hormonal imbalance and/or systematic diseases *(3)*. Hypothyroidism, hypogonadism, hypopituitarism,

■ Shady Elbeshry,
■ Tarek Hassan Abdelaziz,
■ Ahmad Saeed Aly,
■ Shady Mahmoud.
Ain Shams University Hospitals, Ramses St., Abbasiya sq., 11566 Cairo, Egypt.
Correspondence : Dr. Shady Mahmoud, Ain Shams University Hospitals, Ramses St., Abbasiya sq., 11566 Cairo, Egypt. Phone: (+2)1094064223.
Email : dr.shadi87@hotmail.com

No benefits or funds were received in support of this study.
None of the authors have a conflict of interest.

renal osteodystrophy (ROD) as well as radiation exposure have been incriminated individually to be involved in SCFE pathogenesis *(5)*.

Vitamin D is a fat-soluble vitamin that regulates calcium and phosphorus homeostasis. It has a stimulatory effect on chondrocyte proliferation, both directly and by acting on local insulin-like growth factor (IGF). Furthermore, it interacts with parathyroid hormone (PTH) and growth hormone - insulin growth factor-1(GH-IGF-1) pathway, promoting physeal growth with subsequent closure *(6)*.

There is a rising link between vitamin D deficiency and SCFE development observed primarily by the seasonal variation feature of SCFE prevalence *(1,7,8)*. In 2010, Skelly et al. *(9)* spotted the light on this issue by describing an African American boy who has severe bilateral SCFE with severe vitamin D deficiency. They noticed the absence of physeal closure or osteotomy healing after in situ pinning and subtrochanteric valgus osteotomy, except after correction of vitamin D level. Vitamin D level was not routinely measured in SCFE work-up in the United States before this study. Therefore, they recommended early detection and proper treatment of vitamin D deficiency to assess the treatment of SCFE. Madhuri et al. *(10)* described vitamin D deficiency in all except one of 15 cases with SCFE, while the control group showed deficiency in one patient of 15 individuals.

To our knowledge, no study has addressed the effect of severity of vitamin D deficiency on the degree of SCFE slippage as well as on bilateral development. Our study tries to answer both of these questions and investigates the benefits of vitamin D correction before surgery to avoid possible complications related to bone healing and union of the osteotomy as well as physeal closure, which obviously prevents further slip. Therefore, a prospective case series study was conducted.

MATERIALS AND METHODS

This is a prospective, non-randomized case series study that was conducted on human participants with the approval of the Human Research Ethical Committee. It was performed between 2016 and 2019, at our university hospital, and followed-up over 12-48 months (mean 26 months). There were 39 patients (29 males and 10 females) with chronic moderate-severe stable SCFE. Eleven of them had had in situ pinning elsewhere with closed physis and they came to us for the osteotomy. The remaining 28 were presented without prior operations. Of them, the physis status was closed in five (received osteotomy only), and open/closing in 23 who received a staged fashion surgery [table 1].

Thorough preoperative assessment that involved clinical assessment, history taking (especially medication history that affects vitamin D metabolism as antiepileptic drugs) and clinical examination was performed. Radiological assessment included plain x ray and CT scan. In addition, serum levels of T3, T4, TSH as well as circulating form of vitamin D (25(OH) D_3) were measured in every patient. The correlation between SCFE development and vitamin D deficiency was evaluated. The level of vitamin D was compared to the degree of SCFE slippage severity, based on Southwick angle degree, as well as the bilateral development of SCFE to find out any correlation.

Patients with preoperative vitamin D deficiency, evidenced by vitamin D level below 30 ng/mL *(11)*, received an intramuscular course of vitamin D prior to proceeding to the definitive surgery. The course was 200.000 IU of vitamin D3 "Cholecalciferol", once every two weeks. Two weeks after the third dose, vitamin D level was repeated to ensure that normal values had been achieved. In case of persistent deficiency, repeated doses and testing were done until a normal level of vitamin D was reached. In situ pinning was done as first stage surgery in 23 patients, while five patients were presented with closed physis and 11 patients had pinning elsewhere before their presentation to our center. The osteotomy surgery *(12)* was delayed until normal vitamin D levels were achieved.

After surgery, radiographs were performed to assess the osteotomy healing at six weeks, three months, six months, 12 months, and then at the end of the final follow-up. Physis closure was also monitored in 23 patients (59% of the population) who received first stage in situ pinning surgery as vitamin D correction was commenced concomitantly with the surgery.

Table 1. — Patients' demographics

		Total patients = 39
Age	Mean ± SD Range	15.15 ± 1.63 12-18
Gender	Female Male	10 (25.64 %) 29 (74.35 %)
Treated patients	Bilateral Unilateral	19 (48.7 %) 20 (51.28 %)
Severity	Severe Moderate	31 (79.84 %) 8 (20.5 %)
Physis status	Closed Closing Open	16 (41%) 12 (30.76 %) 11 (28.2%)
Previous operation	Positive Negative	11 (28.2 %) 28 (71.8 %)

RESULTS

Thirty-eight patients demonstrated vitamin D deficiency preoperatively evidenced by low serum level of 25(OH) D_3. The range of vitamin D deficiency was between 4.33 and 27 ng/mL with a mean value of 14.39 ng/mL. One of these patients was on regular sodium valproate for epilepsy; he developed SCFE despite his normal BMI (20.2). Only one patient had a normal vitamin D level that was 59.3 ng/mL. All patients had a normal thyroid profile.

No correlation existed between the severity of vitamin D deficiency and the slip severity with a correlation coefficient of -0.031 (p value 0.85). A slight negative correlation existed between the level of vitamin D and the bilateral development of SCFE with a correlation coefficient of -0.213 (p value 0.192). The correlation that was not statistically significant [Table 2 and Figure 1].

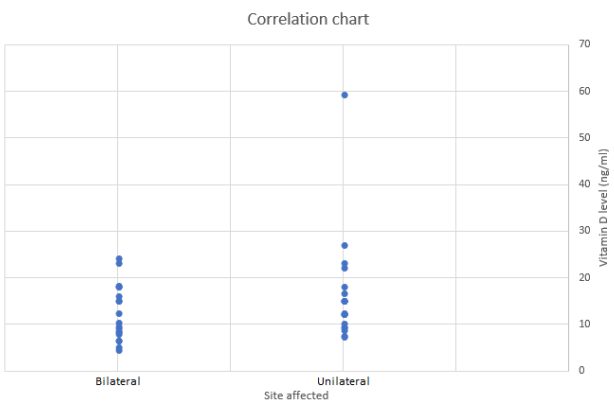

Figure 1. — Correlation chart between vitamin D level and SCFE bilaterality.

Table 2. — Preoperative vitamin D level in relation to SCFE severity and bilaterality in each patient

Number	Site	Southwick angle (severity)	Vitamin D (ng/ml)
1	Bilateral	54	4.33
2	Bilateral	58	9.1
3	Left	50	27
4	Bilateral	84	18.2
5	Left	42	23
6	Bilateral	64	15
7	Bilateral	48	6.5
8	Bilateral	60	12.3
9	Left	52	7.3
10	Bilateral	67	8.3
11	Left	82	15
12	Bilateral	51	18
13	Bilateral	83	16
14	Right	58	12
15	Right	41	9.2
16	Bilateral	65	15
17	Right	62	59.3
18	Right	46	9.3
19	Right	55	12
20	Left	59	15
21	Bilateral	60	6.5
22	Right	50	12
23	Bilateral	57	8.5
24	Left	53	12.2
25	Bilateral	52	23
26	Left	52	15
27	Right	53	18
28	Bilateral	75	5
29	Bilateral	65	7.8
30	Left	45	15
31	Bilateral	60	10.3
32	Right	41	8.6
33	Right	70	7.5
34	Bilateral	53	9.5
35	Bilatera	52	18
36	Left	53	16.5
37	Right	40	22
38	Bilateral	50	24
39	Left	53	10

Postoperatively, osteotomy healing was complete in all patients by the end of the 3rd month. Physis closure was complete in patients who received first stage in situ pinning surgery at 12 months follow-up, and no patient had further progress of the slip.

DISCUSSION

There are several evidences increasing a relationship between vitamin D deficiency and the development of SCFE. Several studies have described seasonal variations in SCFE *(1,7,8)*. They did not identify a specific etiological explanation for this feature, but vitamin D deficiency, a result of insufficient sunlight exposure, and increased weight during these months were accused *(7)*. Recently, Loder et al published the largest ever study with 10350 patient records over 10 years. They described for the first time a double peak in the areas between 31^0-35^0 latitudes and a peak above 35^0 latitudes; nevertheless, no variation existed below 30^0 latitudes. They also found a correlation between the variations and climate. Areas with a humid cold climate demonstrated seasonal variations in comparison to the hot arid ones. The same trend in areas with sun exposure <2500 hours per year compared to the sunny areas. The incidence of SCFE reached the highest in mid-August, but no difference with various ethnic or gender groups *(8)*.

Based on the facts that vitamin D level in children vary throughout the year and the difference of SCFE incidence in relation to sunlight exposure, a link was established between vitamin D deficiency and SCFE occurrence *(13)*. This supports the view of authors who believe that SCFE represents a state of subclinical rickets with defective physeal mineralization *(14,15)*.

Skelly et al. *(9)* discovered severe vitamin D deficiency in an African American boy with severe bilateral SCFE. They noticed the absence of physeal closure or osteotomy healing after subtrochanteric valgus osteotomy except after correction of the vitamin D profile. Therefore, they recommended early detection and proper treatment of vitamin D deficiency to ensure normal bone formation and healing.

Jinguishi et al. *(16)* also depicted a transient decline in the active form of vitamin D, 1,25(OH) D3, among 13 children with SCFE, indicating that it may have an association with SCFE occurrence. In 2013, Madhuri et al. *(10)* detected an incidence of vitamin D deficiency at 93% among 15 cases with an average level of 11.87 ng/mL, while its level in the control group was deficient in only 6.66%.

Judd et al. *(17)* described a negative correlation between vitamin D level and the time needed for physis closure after in situ pinning and commenced on regular assessment of vitamin D level throughout the treatment period with vitamin D supplementation when necessary.

Vitamin D deficiency was even incriminated to have a role in re-slippage of a previously fixed SCFE case with a pin in a case report study by Haque et al. *(18)*.

Moreover, vitamin D deficiency is more common among obese than non-obese individuals, attributed to vitamin D sequestration in fatty tissue, decreasing the available active vitamin D *(13,19)*. Reinehr et al witnessed significantly higher PTH and lower vitamin D in obese individuals compared to non-obese ones confirming this link *(19)*.

Based on the above, the link between vitamin D deficiency and development of SCFE has been well established, but no previous study in English literature has found a correlation between the degree of deficiency and the degree of SCFE slippage or bilateral development.

To our knowledge, our study is the first study to assess such correlations. We did not find a link between the severity of vitamin D level and the slip severity, but a link existed between the vitamin D level and bilateral development, although not statistically significant.

As evidenced by the osteotomy healing and physeal closure in all patients as well as no patient developing a progress of slip, this study goes in line with what Skelly et al. *(9)* and Judd et al. *(17)* confirm regarding the importance of vitamin D level assessment in SCFE patients and treatment of any deficiency.

CONCLUSION

We recommend adopting vitamin D level assessment in the preoperative work-up and to treat

vitamin D deficiency once diagnosed and before proceeding to the definitive surgical intervention of SCFE patients in order to lessen the complications related to bone healing (union of the osteotomy and physeal closure) and to treat a possible cause of the disease. However, pinning in situ should not be postponed.

REFERENCES

1. Lehmann C, Arons R, Loder R, Vitale M. The Epidemiology of Slipped Capital Femoral Epiphysis : An Update. Journal of Pediatric Orthopaedics. 2006;26(3):286-90.
2. Southwick W. Compression fixation after biplane intertrochanteric osteotomy for slipped capital femoral epiphysis. A technical improvement. Journal of Bone and Joint Surgery, Am. 1973;55(6):1218-1224.
3. Witbreuk M, van Kemenade FJ, Van Der Sluijs JA, Jansma EP, Rotteveel J, van Royen BJ. Slipped capital femoral epiphysis and its association with endocrine, metabolic and chronic diseases : a systematic review of the literature. J Child Orthop. 2013,213-23.
4. Loder RT, Aronsson DD, Dobbs MB, Weinstein SL. Slipped capital femoral epiphysis. JBJS. 2000 Aug 1;82(8):1170.
5. Herngren B, Stenmarker M, Vavruch L, Hagglund G. Slipped capital femoral epiphysis : a population-based study. BMC musculoskeletal disord. 2017;18(1):304.
6. Klaus G, Weber L, Rodriguez J, et al. Interaction of IGF-I and 1 alpha, 25(OH)2D3 on receptor expression and growth stimulation in rat growth plate chondrocytes. Kidney Int. 1998;53(5):1152-61.
7. Brown D. Seasonal Variation of Slipped Capital Femoral Epiphysis in the United States. Journal of Pediatric Orthopaedics. 2004;24(2):139-43.
8. Loder RT, Schneble CA. Seasonal Variation in Slipped Capital Femoral Epiphysis : New Findings Using a National Children's Hospital Database. Journal of Pediatric Orthopaedics. 2019 Jan 1;39(1):e44-9.
9. Skelley NW, Papp DF, Lee RJ, Sargent MC. Slipped capital femoral epiphysis with severe vitamin D deficiency. Orthopedics. 2010;33:921.
10. Madhuri V, Arora SK, Dutt V. Slipped capital femoral epiphysis associated with vitamin D deficiency: a series of 15 cases. Bone Joint J. 2013;95-B:851-854.
11. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96:1911-1930.
12. Abdelaziz TH, Elbeshry SS, Goda AH, Fayyad TA, Aly AS, Mahmoud SA. Intertrochanteric Imhäuser osteotomy combined with osteochondroplasty in treatment of moderate-severe stable slipped capital femoral epiphysis: a case series study. Journal of Pediatric Orthopaedics B. 2020 May 1;29(3):283-91.
13. Alemzadeh R, Kichler J, Babar G, Calhoun M. Hypovitaminosis D in obese children and adolescents : relationship with adiposity, insulin sensitivity, ethnicity, and season. Metabolism. 2008;57:183–91.
14. Loder RT. A worldwide study on the seasonal variation of slipped capital femoral epiphysis. Clin Orthop Relat Res. 1996;322: 28-36.
15. Farrier AJ, Ihediwa U, Khan S, et al. The seasonality of slipped upper femoral epiphysis - meta-analysis: A possible association with vitamin D. HIP Int. 2015;25(6):495-501.
16. Jingushi S, Hara T, Sugioka Y. Deficiency of a parathyroid hormone fragment containing the midportion and 1,25-dihydroxyvitamin D in serum of patients with slipped capital femoral epiphysis. J Pediatr Orthop.1997, 17:216-219.
17. Judd J, Welch R, Clarke A, Reading IC, Clarke NM. Vitamin D Deficiency in Slipped Upper Femoral Epiphysis. Journal of Pediatric Orthopaedics. 2016;36(3):247-52.
18. Haque AU, Bloch B, Abraham A. Reslip of a Previously Fixed Slipped Upper Femoral Epiphysis with an Associated Vitamin D Deficiency. Case Rep Orthop . 2014;1-2.
19. Reinehr T, de Sousa G, Alexy U, Kersting M, Andler W. Vitamin D status and parathyroid hormone in obese children before and after weight loss. Eur J Endocrinol. 2007;157(2):225-32.