Abstract

Background

Slipped upper femoral epiphysis (SUFE) has an incidence of 1-7 per 100,000 adolescents in the UK and its link with obesity well established. With a rising number of paediatric orthopaedic patients presenting with vitamin D deficiency, the aim of our study was to establish the prevalence of vitamin D deficiency in SUFE patients presenting to an orthopaedic department in the UK and whether a low vitamin D level increases the time to proximal femoral physeal fusion, post-surgical fixation.

Methods

A total of 27 paediatric patients, with a female to male ratio of 17:10 and a mean age of 11.5 years (SD 1.99), range 8 to 16 years, presented with a SUFE and had their vitamin D level assessed during the study period, June 2007 to July 2012 (inclusive). The majority of these patients (85.2%) were assessed as vitamin D deficient, with a serum 25-(OH)D <52 nmols/L . The time taken for >50% physeal fusion on anteroposterior radiography post-surgical fixation quoted in the literature is 9.6 months with no reported vitamin D deficiency or insufficiency.

Results

In our study the median time to physeal fusion in the vitamin D deficient and insufficient patients was 25 months, interquartile range 17-43 (mean of 29 months, SD 16.8). A negative correlation was also observed between vitamin D level and the time taken for physeal fusion following surgical fixation.

Conclusion

We conclude that a high prevalence of vitamin D deficiency has been observed in our SUFE patients. Comparing the time taken for physeal closure as 9.6 months in the literature with vitamin D deficient patients, this is prolonged. Indeed a negative correlation between vitamin D level and time to physeal fusion has been demonstrated. This study highlights the need for regular vitamin D status assessment in SUFE patients in order to allow early implementation of treatment with vitamin D supplementation. The impact of vitamin D screening and supplementation on SUFE outcomes should be investigated further.

Introduction

Slipped upper femoral epiphysis (SUFE) was first described by Ambroise Paré in 1575 1 and is a well-recognised disorder of adolescent hips, characterised by displacement of the capital femoral epiphysis through the physeal plate from the femoral neck, such that the femoral neck is displaced anteriorly. 2, 3 Whilst the aetiology of most SUFE cases is unknown, 2,4,5 associations have been made with some endocrine disorders 3, 6, 7 and indeed its links with obesity are well documented. 3,8,9,10,11,12

Figure 1

In the UK, childhood obesity has doubled in the last 20 years, with estimations in 2010 that 30% of UK children are obese. 13 Murray and Wilson 8 found a correlation between increased SUFE incidence with obesity in Scotland, from 3.78 to 9.66 per 100,000 in the last two decades and also noted a lower mean age of children with a SUFE diagnosis.

Recent observations have also illustrated a growing number of paediatric orthopaedic patients presenting with vitamin D deficiency or insufficiency in the UK.14, 15 Davies et al 14 noted 32% of paediatric orthopaedic patients had vitamin D insufficiency and 8% were vitamin D deficient, whilst Alemzadeh et al 16 has concluded that vitamin D deficiency is more common in childhood obesity. The rising incidence of vitamin D deficiency has been linked to many musculoskeletal disorders, including a higher incidence of fractures in the paediatric population. 15 Parry et al 17 highlighted the risk of poor bone healing following paediatric orthopaedic surgery in vitamin D insufficient patients and found that 90% of children admitted for orthopaedic surgery had insufficient vitamin D levels.

Likewise SUFE aetiology has also been linked to seasonal variations 18,19,20 and endocrine abnormalities 6, and a case report by Skelley et al 21 in 2010 noted delayed union and pain in an obese SUFE patient who was vitamin D deficient. Madhuri et al 22 also noted a high prevalence of vitamin D deficiency amongst 15 SUFE patients in India. Whilst Jinguishi et al 23 observed a transient deficiency in 1,25-dihydroxyvitamin D in 13 Japanese SUFE patients and concluded that deficiency of the activated form of vitamin D during the growth spurt may result in SUFE development.

SUFE treatment through single cannulated screw in situ pinning aims to halt any further slip, preventing further complications through premature physeal fusion. 2, 4, 24 We hypothesise that the time taken for physeal fusion, (post-surgical fixation), may be prolonged in vitamin D deficient patients, therefore delaying recovery and potentiating further complications. The purpose of this study was to establish the prevalence of vitamin D deficiency in patients presenting with a SUFE and to assess whether the time to physeal fusion was prolonged in vitamin D deficient SUFE patients. This paper presents a retrospective cohort study conducted at a single centre, of consecutive paediatric patients who presented to the orthopaedic department at University Hospital Southampton (UHS), with a SUFE between June 2007 and July 2012.

Patients and Methods

Children who presented to UHS with a SUFE and who underwent a blood test to determine vitamin D levels were included in the study. Paediatric orthopaedic clinic lists identified eligible patients and data was obtained from: patients’ medical notes; hospital computer systems PACs (Picture Archiving and Communication System) and eDocs, up until December 2012. Patients were excluded from analysis: if their vitamin D level (25-(OH)D) was not tested at the time of presentation; they were found to have an endocrine abnormality; developed avascular necrosis (AVN) or were lost to follow-up.

Clinical examination confirmed SUFE diagnosis and this was confirmed by pelvic radiograph (anteroposterior and frog-leg lateral views). Radiographs were taken at the time of the operation and then at an average of eight weeks interval until closure of the physeal plate. Inter observer variation was reassessed by the senior consultant. Physeal fusion was assessed using pelvic radiographs, taken at the time of the surgery and then at an average of eight week intervals until closure of the physeal plate. Two reviewers, not blinded to patient information assessed the radiographs for physeal fusion, defined when >50% of the physis had closed on the anteroposterior radiograph.25

Time to physeal fusion was recorded up until December 2012, although some physes had not fused by that time. For these hips, the length of time since their surgical fixation up until December 2012 was used as an estimate of their time to physeal fusion.

Single cannulated screw in situ pinning is the standard surgical treatment for the majority of SUFE cases at our institution. All patients in this study were treated with this surgical technique by a consultant or senior registrar in paediatric orthopaedic surgery.

Figure 2

Results

During the study period 39 SUFE patients were identified, of whom 34 (87.2%) had their vitamin D level assessed. Of these, seven patients were excluded from analysis: one patient with hypothyroidism, three developed AVN and three were lost to follow-up. This gave 27 patients eligible for analysis, 5 presented with bilateral SUFE and underwent bilateral fixation in a single operation and a further 11 patients developed contralateral SUFE prior to commencing any treatment for vitamin D deficiency, to give a total of 43 hips.

Statistical analysis

Data was analysed using STATA version 11.0. Patient characteristics on presentation were summarised. Although summary statistics were presented for all 43 hips on which data were obtained, further analyses were restricted to the first presenting hip per patient. This was to avoid within-patient similarities in hips impacting and possibly masking the relationships being investigated. In particular, the time to physeal fusion tended to be very similar in pairs of hips within individuals if not identical. Among all patients presenting with bilateral SUFE, their times to physeal fusion were identical in both hips and so just one of these was included in the analysis at random.

Spearman’s rank correlation was used to explore the strength of any pairwise associations between each of time to physeal fusion, vitamin D level, degree of slip and symptom chronology. Regression analysis was used to explore the nature of any relationships indicated by the correlations above. Since the data were highly skewed, regression residuals were examined to check for assumptions of normality and were found to be satisfactory.

The mean age was 11.5 years (SD 1.99) (8 to 16 years), with a female to male ratio of 17:10. Patients’ weights at the time of the operation were placed on an age and gender specific centile growth chart. Twenty six of the twenty seven patients (96.3%) were above the 75th centile, with twenty one patients (77.8%) above the 91st centile.

Each of the 43 SUFE hips were classified in terms of stability, with 38 (88.4%) hips termed stable and 5 (11.6%) unstable. The majority of SUFE patients presented with symptoms greater than 3 weeks and were termed chronic 18 (41.9%), 14 (32.6%) presented in the acute stage (<3 weeks), with 11 (25.6%) defined as acute-on-chronic. In terms of the categorised degree of hip displacement using the posterior sloping angle, the majority 30 (69.8%) were mild, 11 (25.6%) moderate and 2 (4.7%) were severe.

A total of 16 hips had not yet fused by the end of the study period and were therefore estimated as described above to give a conservative underestimate of their time to physeal fusion. The median time to physeal fusion in all 43 hips was 19 months, with an inter-quartile range (IQR) of 8-31 months. Among those who had fused within the study period (n=27), the median time to fusion was 25 months, IQR 17-43 months.

Of the 27 patients, just 2 patients (7.4%) had normal vitamin D levels, 2 patients (7.4%) were vitamin D insufficient, whilst 23 patients (85.2%) were vitamin D deficient. Even those patients with sufficient vitamin D levels, they were only just sufficient, at 73 and 79 nmol/L respectively.

Figure 3

The median time to physeal fusion in hips of patients with vitamin D insufficiency or deficiency was 20 months, (IQR 8-33 months). Among those who had fused within the study period and were vitamin D insufficient or deficient (n=27), the median time to fusion was 25 months, IQR 17-43 months.

Table 1 and 2

Further analysis to explore the relationship between vitamin D levels and time to physeal fusion was restricted to the first presenting hip as previously discussed. A negative correlation was seen between vitamin D levels and time to physeal fusion (Spearman’s Rank correlation -0.378, p=0.052). Furthermore, a regression analysis indicated that an increase of one nmols/L in vitamin D was associated with a decrease in time to physeal fusion of 11 days (95% confidence interval 0.3 to 21 days, p=0.057), suggesting an association between vitamin D levels and time to physeal fusion even in this relatively small sample.

There was no evidence of an association between time to physeal fusion and degree of slip (Spearman’s Rank correlation 0.088, p=0.66) or between time to physeal fusion and symptom chronology. There was evidence of an association between vitamin D level and degree of slip (Spearman’s Rank correlation -0.423, p=0.028), however, this did not alter the relationship observed between time to physeal fusion and vitamin D level when degree of slip was added into a multivariable regression model.

 Discussion

Previous studies have discussed the concern related to premature closure following fixation of SUFE, with the associated problems of greater trochanteric overgrowth, coxa breva and coxa vara. The literature reports an average of 12 - 13 (range, 2-34) months to physeal closure postoperatively 24,25 26. In this study we defined physeal fusion when >50% of the physis had closed on the anteroposterior radiograph, as described by Goodman et al. 26 The mean time taken for >50% physeal closure on anteroposterior radiographs is quoted as 9.6 months in this study. None of the studies made reference to vitamin D deficiency or insufficiency.

Whilst the classification of vitamin D deficiency in children remains controversial,14 in this study the vitamin D (25-(OH)D) level was interpreted using the UHS laboratory reference values, where <52 nmols/L was considered vitamin D deficient and between 52-72 nmols/L to be vitamin D insufficient. These reference values are in keeping with the American institute of medicine classification of vitamin D deficiency and insufficiency. 27 In the UK the optimal vitamin D blood level is currently recommended as 25nmols/L, though there is some agreement that this should be above 50nmols/L 28, a level based on the benefits that have been seen in a number of chronic diseases, including osteoporosis. Currently there is ongoing debate as to the level that constitutes a low vitamin D status for the UK population as a whole, with no evidence based reference value recommended specifically for children.

The potential link between SUFE and nutritional deficiencies with particular focus on vitamin D deficiency is beginning to be considered, with the case study by Skelley et al21 and the series of 15 cases by Madhuri et al. 22 Indeed this was evident in our study from the higher percentage of vitamin D deficient SUFE patients (85.2%), compared to those presenting with a sufficient/normal vitamin D level (7.4%). Direct comparison to other studies which have demonstrated vitamin D deficiency in UK paediatric patients, is difficult, due to the varying range of normal vitamin D reference values, with some hospital laboratories using higher values 29.

Recent observations have illustrated a growing number of paediatric orthopaedic patients presenting with vitamin D deficiency or insufficiency in the UK.14,15 , whilst Alemzadeh et al 16 has concluded that vitamin D deficiency is more common in childhood obesity. The rising incidence of vitamin D deficiency has been linked to many musculoskeletal disorders, including a higher incidence of fractures in the paediatric population. 15 Parry et al 17 has highlighted the risk of poor bone healing following paediatric orthopaedic surgery in vitamin D insufficient patients and found that 90% of children admitted for orthopaedic surgery had insufficient vitamin D levels.

Each SUFE was classified in terms of stability according to Loder et al,30 judged on the ability to weight-bear or not, chronology of symptom onset and the degree of displacement from radiological measurements. Loder et al 30 classification of slip stability was applied, where each slip was termed ‘stable’ or ‘unstable’ due to the ability to weight-bear. The traditional classification of symptom onset chronology was also considered, with symptom duration of three weeks or less referred to as the acute stage and greater than 3 weeks termed chronic. An acute exacerbation on a prolonged background history of symptoms was considered acute-on-chronic. 4 The degree of epiphysis displacement on the femoral neck was measured using the posterior sloping angle on the lateral pre-surgical pelvic radiographs, this was subsequently categorised as mild (0-30 degrees), moderate (30-60 degrees) or severe slips (>60 degrees).31

The increase in SUFE incidence has been acknowledged worldwide with a decrease in the age of SUFE diagnosis, 8,12 as witnessed in our study with the mean age of 11.5 years. The prevalence of vitamin D deficiency amongst paediatric orthopaedic patients has also seen a rise. 14 Of the 27 patients, just 2 patients (7.4%)d normal vitamin D levels, 2 patients (7.4%) were vitamin D insufficient, whilst 23 patients (85.2%) were vitamin D deficient. Even those patients with sufficient vitamin D levels were only just sufficient, at 73 and 79 nmol/L respectively.

Time to physeal fusion was prolonged in our study, with a median of 25 months, IQR 17-43 months in hips of patients who were vitamin D insufficient or deficient (mean of 29 months, SD 16.8). This compares with the literature mean value of 9.6 months among SUFE patients with no reported vitamin D deficiency. 25

This study demonstrated an association between vitamin D deficiency and time to physeal closure (fusion). No other study has reported this finding to date. This finding approached statistical significance (p=0.052) even among this small group of patients. Thus, there is an indication for vitamin D screening in patients presenting with SUFE and for the early implementation of vitamin D supplementation. There was also evidence that vitamin D deficiency was associated with a greater degree of epiphysis displacement (p=0.028), although this did not influence the relationship already observed between time to physeal fusion and vitamin D levels. Hence, low vitamin D levels were associated with both; greater slip severity at presentation as well as prolonged time to physeal fusion, although the slip severity was not independently associated with time to physeal fusion.

Other potential confounding factors that may have influenced the association between time to physeal fusion and vitamin D levels were explored, including symptom chronology. No such associations were found.

This study presents findings on recent consecutive patients seen in an NHS setting over a 5-year period. As such, it is likely to be representative of the wider UK population and forms a reference group for further research.

In this study we had a higher percentage of female patients, this goes against the grain of many other studies and the literature of a higher SUFE prevalence in males. 2,22 However, the reduction in male prevalence has been noted in other work, 12 although not to the extent where female prevalence is higher as observed in our study.

Whilst it would have been useful to have the BMI for these SUFE patients, patients’ height is not routinely measured for surgical pre-assessment at UHS. We therefore elected to place the patients’ weight at the time of the operation on the gender and age specific growth centile chart as an indicator of weight growth. As this was a retrospective study, ideally we would have assessed the time to physeal fusion post-surgical fixation with 6 weekly radiographs, rather than the mean eight week intervals used.

This study has highlighted the potential necessity for routine vitamin D status assessment in SUFE patients, in order to allow the implementation of early treatment with vitamin D supplementation. It may also highlight the need to address the high prevalence of vitamin D deficiency in our paediatric population as a whole. Vitamin D level may also affect the likeliness of slipping on the contralateral side if vitamin D is low, given that 41% of this patient population went on to develop contralateral SUFE. The impact of vitamin D screening and supplementation on SUFE outcomes requires further research in the form of a prospective, adequately powered controlled trial.

Figure 1 Pre-operative images showing showing AP and Frog lateral views of right slipped upper femoral epiphysis.

Figure 2 Immediate post-operative AP and Frog lateral views showing single screw fixation and the open physis.

Figure 3 2 years post operation. AP and frog lateral views show that the physis remains open. The right hip has been prophylactically pinned and the epiphysis is growing off the screw.

**References**

1. Paré A. Oeuvres complètes D’Ambroise Paré: revues et collationées sur toutes les éditions avec les variantées: preceded by an introduction by J. F. Malgaigne, Book 13, Chapter 21, appearing in Tome 2, Chez J. B. Baillière, Paris 1840:326.

2. Loder RT, Aronsson DD, Dobbs MB, Weinstein SL. Slipped capital femoral epiphysis. *J Bone Joint Surg [Am]* 2000;82-A: 1170-1188.

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;7: 213-223.

4. Uglow MG, Clarke NMP. The management of slipped capital femoral epiphysis. *J Bone Joint Surg [Br]* 2004;86-B: 631-635.

5. Loder RT, Dietz FR. What is the best evidence for the treatment of slipped capital femoral epiphysis? *J Pediatr Orthop* 2012;32: S158 – S165.

6. Loder RT, Wittenberg B, DeSilva G. Slipped capital femoral epiphysis associated with endocrine disorders. *J Pediatr Orthop* 1995;15: 349-356.

7. Wells D, King JD, Roe TF, Kaufman FR. Review of slipped capital femoral epiphysis associated with endocrine disease. *J Pediatr Orthop* 1993;13: 610-614.

8. Murray AW, Wilson NI. Changing incidence of slipped capital femoral epiphysis: a relationship with obesity? *J Bone Joint Surg [Br]* 2008;90-B: 92-94.

9. Manoff EM, Banffy MB, Winell JJ. Relationship between body mass index and slipped capital femoral epiphysis. *J Pediatr Orthop* 2005;25: 744-746.

10. Bhatia NN, Pirpiris M, Otsuka NY. Body mass index in patients with slipped capital femoral epiphysis. *J Pediatr Orthop* 2006;26: 197-199.

11. Poussa M, Schlenzka D, Yrjonen T. Body mass index and slipped capital femoral epiphysis. *J Pediatr Orthop B* 2003;12: 369-371.

12. Nguyen AR, Ling J, Gomes B, Antoniou G, Sutherland LM, Cundy PJ. Slipped capital femoral epiphysis: rising rates with obesity and aboriginality in South Australia. *J Bone Joint Surg[Br]* 2011;93-B: 1416-1423.

13. Health Survey for England, 2010. The NHS Information Centre, 2011. Available at:

http://www.ic.nhs.uk/pubs/hse10report

14. Davies JH, Reed JM, Blake E, Priesemann M, Jackson AA, Clarke NMP. Epidemiology of vitamin D deficiency in children presenting to a pediatric orthopaedic service in the UK. *J Pediatr Orthop* 2011;31: 798-802.

15. Clarke NM, Page JE. Vitamin D deficiency: a paediatric orthopaedic perspective. *Curr Opin Pediatr* 2012;24: 46-49.

16. 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: 183-191.

17. Parry J, Sullivan E, Scott AC. Vitamin D sufficiency screening in preoperative pediatric orthopaedic patients. *J Pediatr Orthop* 2011;31: 331-333.

18. Brown D. Seasonal variation of slipped capital femoral epiphysis in the United States. *J Pediatr* Orthop 2004;24: 139-143.

19. Lehmann CL, Arons RR, Loder RT, Vitale MG. The epidemiology of slipped capital femoral epiphysis: an update.  *J Pediatr Orthop* 2006;26: 286-290.

20. Loder RT. A worldwide study on the seasonal variation of slipped capital femoral epiphysis. *Clin Orthop Relat Res.* 1996; (322): 28-36.

21. Skelley NW, Papp DF, Lee RJ, Sargent MC. Slipped capital femoral epiphysis with severe vitamin D deficiency. Orthopedics 2010;33: 921.

22. Madhuri V, Arora SK, Dutt V. Slipped capital femoral epiphysis associated with vitamin D deficiency. *Bone Joint J* 2013;95-B: 851-854.

23. 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.

24. Stanton RP, Shelton YA. Closure of the physis after pinning of slipped capital femoral epiphysis. *Orthopedics* 1993;16: 1099-1102.

25. [Ward WT](http://www.ncbi.nlm.nih.gov/pubmed?term=Ward%20WT%5BAuthor%5D&cauthor=true&cauthor_uid=1634570), [Stefko J](http://www.ncbi.nlm.nih.gov/pubmed?term=Stefko%20J%5BAuthor%5D&cauthor=true&cauthor_uid=1634570), [Wood KB](http://www.ncbi.nlm.nih.gov/pubmed?term=Wood%20KB%5BAuthor%5D&cauthor=true&cauthor_uid=1634570), [Stanitski CL](http://www.ncbi.nlm.nih.gov/pubmed?term=Stanitski%20CL%5BAuthor%5D&cauthor=true&cauthor_uid=1634570).Fixation with a single screw for slipped capital femoral epiphysis. [J Bone Joint Surg Am.](http://www.ncbi.nlm.nih.gov/pubmed/1634570) 1992 Jul;74(6):799-809.

26. Goodman WW, Johnson JT, Robertson WW Jr. Single screw fixation of acute and acute-on-chronic slipped capital femoral epiphysis. *Clin Orthop* 1996;322: 86-90.

27. Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: The National Academies Press; 2011.

28. Joseph B. Vitamin D in children: Frequently asked questions about Vitamin D in children. [www.rnoh.nhs.uk/clinical-services/paediatric-adolescents/vitamin-d-children](http://www.rnoh.nhs.uk/clinical-services/paediatric-adolescents/vitamin-d-children). Accessed August 2014.

29. British paediatric and Adolescent Bone Group. 2012. Position Statement on Vitamin D. <http://bpabg.co.uk/position-statements/vitamin-d-and-fractures>. Accessed August 2014.

30. Loder RT, Richards BS, Shapiro BS, Rezanick LR, Aronson DD. Acute slipped capital femoral epiphysis: the importance of physeal stability. *J Bone Joint Surg [Am]* 1993;75-A: 1134-1140.

31. Phillips PM, Phadnis J, Willoughby R, Hunt L. Posterior Sloping Angle as a Predictor of Contralateral Slip in Slipped Capital Femoral Epiphysis. *J Bone Joint Surg [AM]* 2013;95: 146-150.