Vitamin D status and recommendations in Paediatric Inflammatory Multisystem Syndrome Temporarily associated with SARS-CoV-2 (PIMS-TS)

JR. BRIGHOUSE[1†], M. WAN[1,2†], EL. DUNCAN[3], J. HANDFORTH[1], J. KENNY[1], MZ. MUGHAL[4,5], S. RIPHAGEN[1], P. THEOCHARIS[1], MS. CHEUNG[1]

[†]*These authors have contributed equally to this work and share first authorship*

[1] Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK

[2] Institute of Pharmaceutical Science, King's College London, UK

[3]Department of Twin Research & Genetic Epidemiology, School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London, London, UK

[4]Department of Paediatric Endocrinology & Metabolic Bone Diseases, Royal Manchester Children's Hospital, Manchester, UK

[5]Faculty of Biology, Medicine and Health, University of Manchester, Oxford Road, Manchester, UK

ESPE 2021
The 59th Annual Meeting Online
22-26 September 2021

INTRODUCTION

Paediatric Inflammatory Multisystem Syndrome Temporarily associated with SARS-CoV-2 (PIMS-TS) is a post-infectious phenomenon with life-threatening cardiac complications.(1) Early on, it was noted that many of these children had low 25-hydroxyvitamin D (25(OH)D) concentrations. Beyond its primary role in maintaining calcium and phosphate homeostasis, vitamin D has recognised roles in immunity and inflammation and association between low vitamin D status and Kawasaki disease, which has overlapping clinical features, has also been reported.(2-4)

AIM

The aim of our study was to describe the baseline serum 25(OH)D concentrations in children presenting with PIMS-TS and examine its association with clinical severity. As there is currently minimal data to support an optimal dose to achieve adequate correction of vitamin D concentrations quickly without toxicity in children, particularly in those that are acutely critically unwell, we also describe the efficacy of single high dose vitamin D in the rapid and safe correction of serum 25(OH)D to concentrations >75 nmol/L.

METHOD

We retrospectively analysed data from 109 children (aged 1-18 years) with PIMS-TS admitted to a tertiary paediatric hospital between 16 April 2020 and 31 January 2021. Baseline serum 25(OH)D concentrations were measured and associations with ethnicity, inflammatory markers and myocardial function were assessed. Initially a single dose of 100,000 international units (IU) cholecalciferol was administered to all children on hospital admission, subsequently increased to 200,000 IU, with assessment of post-treatment serum 25(OH)D and calcium.

RESULTS

One hundred and nine children were included in this study; median age was 8.9 years, 68 (62.4%) were male, and 53 (48.6%) were of Black or Asian ethnicity. Median baseline 25(OH)D concentration was 36 nmol/L (Figure 1); 75 (69%) had concentrations <50 nmol/L. Multivariable regression analysis demonstrated significant associations of older age, black/Asian ethnicity, winter months, laboratory evidence of SARS-CoV-2 exposure, and paediatric intensive care unit (PICU) admission with lower 25(OH)D concentrations. Lower 25(OH)D concentrations were associated with raised markers of inflammation including ferritin (R=-0.48; p<0.001), elevated D-Dimer (R=-0.37; p<0.001), and lymphopenia (R=0.41; p<0.001); and evidence of myocardial dysfunction on echocardiogram (Table 1). The proportion of children who achieved post-dose concentrations >75nmol/L in the 100,000 IU and 200,000 IU group were 30% (8/27) and 89% (17/19), respectively (Figure 2). No adverse effects of supplementation were reported in either group.

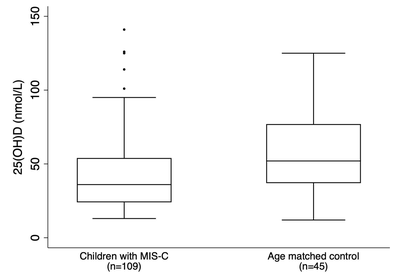

Figure 1: Admission 25(OH)D concentrations in PIMS-TS patients compared to age-matched control patients admitted during the same period

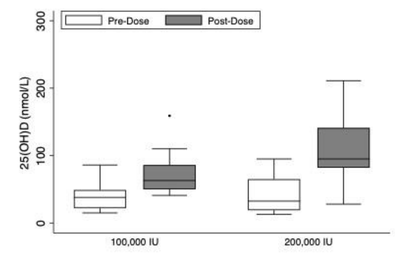

Figure 2: Short term 25(OH)D response to cholecalciferol supplementation (only patients with post-dose 25(OH)D concentrations measured within 7 to 28 days of dosing are included).
100,000 IU group (n = 27); 200,000 IU group (n = 18)

	n (%)	25(OH)D, nmol/L	*p*
Fractional shortening [a]			
< 29%	37 (36.3)	25 (16 - 40)	<0·001
≥ 29% (normal)	65 (63.7)	46 (32 - 68)	
Global longitudinal strain [b]			
≥ -18%	39 (54.9)	25 (15 - 39)	<0·001
< -18% (normal)	32 (45.1)	48 (32 - 70)	
Coronary dilatation [a]			
z-score > 2.5	30 (29.4)	32 (16 - 54)	0.30
z-score ≤ 2.5 (normal)	72 (70.6)	39 (25 - 56)	

Table 1: Association between baseline 25(OH)D concentrations and echocardiographic parameters 25(OH)D data are presented as median and interquartile range in parenthesis. [a] Missing data = 7 [b] Missing data = 38

CONCLUSIONS

The majority of children presenting with PIMS-TS have a low baseline 25(OH)D concentration, which is associated with PICU admission and cardiac dysfunction. Rapid correction of serum 25(OH)D to concentrations >75 nmol/L can be achieved with a single dose of 200,000 IU of oral cholecalciferol for children >one year old, with no children developing hypercalcaemia or hypervitaminosis. Vitamin D could be used as a biomarker of cardiac dysfunction and disease severity in PIMS-TS. An adequately powered multicentre randomised control trial is required to determine if early optimisation of vitamin D status improves outcome of patients with PIMS-TS.

REFERENCES

1. **Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al**. Clinical Characteristics of 58 Children with a Pediatric Inflammatory Multisystem Syndrome Temporally Associated with SARS-CoV-2. *JAMA - J Am Med Assoc* 2020; 324(3): 259-269
2. **Panfili FM, Roversi M, D'Argenio P, Rossi P, Cappa M, Fintini D**. Possible role of vitamin D in Covid-19 infection in pediatric population. *J Endocrinol Invest* 2021; 44(1): 27-35
3. **Feketea G, Vlacha V, Bocsan IC, Vassilopoulou E, Stanciu LA, Zdrenghea M**. Vitamin D in Corona Virus Disease 2019 (COVID-19) Related Multisystem Inflammatory Syndrome in Children (MIS-C). *Front Immunol* 2021; 12: 648546
4. **Xu WR, Jin HF, Du JB**. Vitamin D and Cardiovascular Risk in Children. *Chin Med J* 2017; 130(23):2857-2862

ACKNOWLEDGEMENTS

Thanks to Agata Sobczynska-Malefora and Sally Brady in clinical chemistry at Evelina. We would also like to acknowledge the wider PIMS-TS team, particularly Dr Francesca Davis and Dr Michael Carter for their help with data collection.

CONTACT INFORMATION

James Robert Brighouse
Evelina London Children's Hospital, St Thomas' Hospital
London, SE1 7EH United Kingdom
Tel: +44 7787842692
Email: james.brighouse@nhs.net