

Nutritional Rickets During the COVID-19 Pandemic in Rivers State, Nigeria: A Case Series Highlighting Challenges in Management in A Resource-Constrained Setting

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ABSTRACT

Background: Nutritional rickets (NR) is a global preventable disease of public health significance which negatively affects the growth and development of infants, children and adolescents. NR results from insufficient sunlight exposure, Vitamin D and/or calcium deficiencies. Diagnosis is based on a combination of clinical, biochemical and radiological abnormalities. Treatment with Vitamin D and/or calcium supplementation, and food fortification is efficacious in managing the metabolic disorder. Treatment challenges in resource-limited settings include financial constraints, high costs of diagnostic workup, lack of readily available diagnostic laboratories and high rate of loss to follow-up. Recently, an increasing prevalence has been attributed to the impact of the COVID-19 pandemic due to prolonged movement restrictions and indoor confinement, particularly in young infants and adolescents.

Methods: This is a retrospective review of three Nigerian children who presented to the Endocrinology clinic of the Rivers State University Teaching Hospital with clinical, biochemical and radiological features suggestive of NR. Two of the cases were 42-month-old males while the third case was a 30-month-old female. All received vitamin D and calcium supplementation, however, response to treatment was mostly inadequately monitored due to lost to follow up.

Conclusion: Nutritional rickets among children in Rivers State is on the increase and perhaps is a consequence of COVID-19 pandemic restrictions and worsening nutritional status due to rising inflation in the country. Paediatricians and healthcare workers are hereby alerted to have a heightened index of suspicion to screen and treat nutritional rickets among children with features of nutritional deficiencies with or without overt bony deformities.

Keywords: Nutritional Rickets, Vitamin D Deficiency, COVID-19 Pandemic, Inflation

INTRODUCTION

Nutritional rickets (NR) is a disease of public health significance predominantly affecting growing children due to inadequate vitamin D and/or calcium intake, and reduced exposure to sunlight resulting in defective chondrocyte differentiation and mineralization of the osteoid matrix.¹⁻⁴ The highest prevalence is seen in young children

aged 6-23 months and adolescents 12-15 years.³

Vitamin D is essential for calcium absorption and utilization. When there is a low calcium level, it also stimulates the release of parathyroid hormone, which promotes bone resorption.³ Natural sunlight is the primary source of vitamin D, as vitamin D₃ is produced in the human skin

after exposure to ultraviolet B (UVB) light.^{2,5,6} Vitamin D can also be found in foods such as mackerel, salmon, and fortified formula milk or cereals. Global consensus recommendations on the prevention and management of nutritional rickets recommend a daily vitamin D intake of 400 IU (10 g) for infants and 600 IU (15 g) for children and adults.⁷

Before the COVID-19 pandemic, the global prevalence of nutritional rickets varied greatly ranging from less than 1% to over 50% depending on the geographical location and from differences in diagnostic techniques used, which only included clinical diagnoses or medical imaging and biochemical investigations in some studies.⁴ Non-pharmaceutical interventions such as national lockdowns, travel restrictions, and school closures were used by governments around the world to combat the COVID-19 pandemic.^{8,9} Lockdowns and school closures, while effective in reducing COVID-19 cases, have been shown to have a negative impact on children's health and well-being.¹⁰ With the advent of the pandemic, several reports from both developing and developed countries around the world indicate a significant increase in the prevalence of nutritional rickets.¹¹⁻¹⁴

This case series on nutritional rickets in Nigerian Children in Port Harcourt City, Rivers State is aimed at highlighting a rising prevalence of nutritional rickets possibly due to the impact of the COVID-19 pandemic and worsening nutritional status due to rising inflation in this environment.

CASE PRESENTATIONS

Case 1:

UND is a 3 year 6 months old male, 2nd of a set of twins who presented to the Endocrine unit of this facility with complaints of inward bending of both knees was noticed 1 year ago. There was no history of pain on both limbs, no associated swellings, no prior history of trauma and no medication had been given before presentation. Parent brought child for expert management. Significant aspects of history

were noted to be poor nutritional history; UND was fed only thrice a day with whatever was available. Feeds were not fortified, predominantly on 1 or 2 classes of food – carbohydrates made from a maize gruel (pap) to which half cube of sugar was added when available. Feeds were largely deficient in dairy and animal sources, no fruits or vegetables or other mineral and vitamin sources were added. Mother had stopped breastfeeding over 2 years ago. UND is the second of a set of twin boys and lives with his single mother in a make-shift residence in the suburbs of Port Harcourt city. There was no financial support from their biological father who was at large. During the restrictions in the pandemic child was locked in doors for over 6 months, mother claimed she only came out at night in search of any food item she could afford to make a meal. She was unemployed and largely dependent on external financial assistance. Following child's complaint, no medical intervention was sought due to financial constraints. UND, was however, brought to this facility by members of a Christian charity organization. Significant findings on examination at presentation, were that he was small for age with frontal bossing, height 93cm (<5th percentile stature for age and sex), weight was 11.3kg (< 5th Percentile weight for age and sex), not pale, not in respiratory distress or jaundiced, no significant lymph node swellings. Musculoskeletal examination revealed, bilateral genu valgus with wind swept deformity, rickety rosary with a sulcus on the left chest wall, widening of both wrists and the femurs. A clinical diagnosis of Rickets probably nutritional, was made. Results of serum calcium, phosphate, alkaline phosphatase and 25-hydroxy-vitamin D levels are shown in table 1. Report of X-ray of the femur and tibia done showed there is cupping, splaying and fraying of the distal femoral and proximal tibial and fibular metaphyses, with lateral deviation of the distal tibia. (Figure 1)

Case 2:

UNE is a 3 year 6 months old male, 1st of a set of twins who presented to the Endocrine unit of this facility with complaints of toe walking and inward bending of both knees was noticed 1 year ago. There was no history of pain on both limbs, no associated swellings, no prior history of trauma and no medication had been given before presentation. Other significant aspects of history which differed from his sibling (case 1), were that UNE did not cry well at birth and had delayed developmental milestones compared to twin brother. Significant findings on examination at presentation, were that he was small for age with frontal bossing, height was 90cm (<5th percentile stature for age and sex), weight was 11kg (<5th percentile weight for age and sex), not

pale, not in respiratory distress or jaundiced, no significant lymph node swellings. Musculoskeletal examination revealed, toes walking, bilateral genu valgus with wind-swept deformity, widening of wrist and knees joints, rickety rosary on the anterior chest wall, asymmetrical flattening of the skull with microcephaly, there was normal tone in the limbs. A clinical diagnosis of Rickets probably nutritional in a child with possibly background cerebral palsy was made. Results of serum calcium, phosphate, alkaline phosphatase and 25-hydroxy-vitamin D levels are shown in table 1. Report of X-ray of the femur and tibia done showed there is cupping, splaying and fraying of the distal femoral and proximal tibial and fibular metaphysis, with lateral deviation of the distal tibia. (Figure 1)

Table 1:				
CASE 1				
	Reference ranges	23/08/2020	11/03/2021	23/08/2021
Calcium	2.2 – 2.75mmol/L	2.25	2.06	2.20
Magnesium	0.6 – 1.07 mmol/L	0.86	0.93	-
Phosphate	0.87 – 1.5 mmol/L	2.8	2.17	-
Alkaline phosphatase	150 – 420U/L	4078	-	-
25-OH Vit D	<12ng/ml---Deficiency 12-20ng/ml---Insufficiency >20ng/ml---Sufficient	-	-	15.0
CASE 2				
	Reference ranges	23/08/2020	11/03/2021	23/08/2021
Calcium	2.2 – 2.75mmol/L	2.43	-	2.24
Magnesium	0.6 – 1.07 mmol/L	0.81	-	-
Phosphate	0.87 – 1.5 mmol/L	2.7	-	-
Alkaline phosphatase	150 – 420U/L	1434	-	-
25-OH Vit D	<12ng/ml---Deficiency 12-20ng/ml---Insufficiency >20ng/ml---Sufficient	-	-	21.0



Figure 1: xray of the UND (case 1) and UNE (case 2)

Case 3:

ELO is a 2-year, 6 months old female who presented to the Endocrine unit of this

facility with complaints of abnormal deviation of her legs and abnormal gait of >18 months duration. She was unable to

climb or come down stairs without support. She was said to be weak and needed support when walking. She was born via an elective C-section at term following an uneventful gestation. Birth weight was 2.8kg. She cried well after birth. She was mixed fed from birth and thereafter complimentary feeds were commenced from about 6 months with mostly plant-based meals. ELO was currently on family diet, fed about two to three times a day from mainly 2 – 3 food groups because she was a picky eater. She was a nursery school pupil and spent most of her time indoors as she preferred indoor play activities. She was the first of a set of twins. Other twin-EO is apparently well but mother also concerned about child's vitamin D status. His weight was 10.9kg and height was 88cm (both of which were on the 25th percentile for weight and stature for age and sex). ELO initially was reviewed by a paediatrician who clinically suspected rickets and was commenced on oral Vitamin

D and calcium supplements for 3 weeks before being referred to the Endocrine unit for expert management.

The significant findings on examination at presentation were that she was underweight, weight was 10kg (5th percentile for weight for age and sex), height was 85cm (10th percentile for stature for age and sex), not pale, not dyspnoeic and frontal bossing. Musculoskeletal examination revealed widening of both wrists, no rickety rosary, bilateral genu valgus. There was normal tone in all limbs but she was unable to come down stairs nor squat without support (? proximal weakness). A clinical diagnosis of Nutritional Rickets-vitamin D deficiency was made. Results of serum calcium, phosphate, alkaline phosphatase and 25-hydroxy-vitamin D levels are shown in table 2. Report of X-ray done showed splaying, fraying of and cupping of ulnar and radial metaphyses. (Figure 2).

CASE 3 ELO			
	Reference ranges	06/05/2022	29/06/2022
Calcium	2.2 – 2.75mmol/L	2.67	2.62
Magnesium	0.6 – 1.07 mmol/L	0.81	0.8
Phosphate	0.87 – 1.5 mmol/L	1.25	-
Alkaline phosphatase	150 – 420U/L	97??	1,018
25-OH Vit D	(<20nmol/L)---Deficiency (30-50nmol/L)--insufficiency (>50nmol/L)---sufficient Optimal---50-124.8nmol/L	-	36.5
CASE 4 EO			
	Reference ranges		29/06/2022
Calcium	2.2 – 2.75mmol/L	-	2.51
Magnesium	0.6 – 1.07 mmol/L	-	1.48
Phosphate	0.87 – 1.5 mmol/L	-	-
Alkaline phosphatase	150 – 420U/L	-	261
25-OH Vit D	(<20nmol/L)---Deficiency (30-50nmol/L)--insufficiency (>50nmol/L)---sufficient Optimal---50-124.8nmol/L	-	74.8



Figure 2: X-ray of the wrists of ELO (Case 3)

RESULTS

Oral Vitamin D at 5000IU daily and calcium supplementations at 500mg daily were commenced for all patients. Parents were counselled and encouraged to give locally available, affordable and culturally acceptable calcium rich foods such as crayfish, milk, eggs and mackerel fish, and increase number of feeds to 5-6 x a day. Parents were counselled to encourage safe outdoor play thus increased daily exposure to sunlight. They were also referred to the hospital's Nutrition unit for dietary counselling and recommendations for a meal plan. Thus they were seen by the dietician in the facility at each clinic visit.

ELO is currently doing well. She's been regular with follow-up. Clinic visit 2 months after commencement of therapy showed she was no longer weak and could now walk without support and easily climb stairs and squat. A repeat X-rays done 5 months after commencement of therapy showed normal findings. ELO's physical examination was essentially normal. Lab investigations within normal.

UNE and UDE, however, have been lost to follow up due to financial constraints.

DISCUSSION

NR is a disorder of defective chondrocyte differentiation and osteoid mineralization, due to low calcium intake and/or vitamin D deficiency.¹ Other types of Rickets: renal, genetically inherited (defects in vitamin D metabolism), familial hypophosphatemia, malignancy.^{1,2,7} Previously, it was reported by Thacher et al¹⁵ that Calcium deficiency was a more significant cause of Rickets than Vitamin D deficiency in Nigerian children. More recent studies show Vitamin D deficiency is the most common cause of Rickets.^{1,12,16} Possible reasons for this observation include urbanization and effect of Pandemic restrictions.^{1,12} NR is prevalent worldwide with Rickets representing 0.2-10% of all cases seen in Endocrinology clinics.^{3,4}

Recently, following the Covid-19 pandemic, there has been a surge of cases.^{2,7,12,14,17} A

study done in China reported in 3600 children seen between 2017-2020, vitamin deficiency was higher in 2020, than in 2017-2019.¹⁴ They concluded that confinement at home due to the pandemic was responsible for this.¹⁴ Similarly, Kang et al reported in 226 children 4-18 years, after 6 months of school closure and home confinement, serum (25(OH)D) levels decreased significantly.¹⁷

Our case series reports two sets of twins born at the start of the pandemic, mostly raised indoors because of pandemic restrictions. Thus, it was not surprising that they had reduced vitamin D levels. The first set of twins, born to single unemployed mother, had a very poor nutritional history which was contributory (low calcium diet). Their mother admitted to keeping them locked indoors mostly due to the pandemic she was not allowed to sell provisions in her roadside store which she eventually lost.

Of the second set of twins, the girl child, ELO, preferred indoor play thus had reduced exposure to sunlight. Though born to parents from a high socio-economic class, she was fed mostly twice a day (? Picky-eater). Also both parents were busy entrepreneurs and were not directly involved in supervision of the children's feeding and play. The twins only recently began going to school. Prior to this they were mostly kept indoors and had minimal exposure to direct sunlight.

The ages at which these children presented is within the peak age range reported by several authors (1-3years).^{4,6,15,16,18} Their clinical features were as reported by several authors.^{2,3,7,19} UNE had delayed developmental milestones for which cerebral palsy was suspected. However, this symptom might very well be due to VDD (Vitamin D deficiency) as reported by some authors.^{2,4-6,12,15,16,18} ELO also presented with inability to navigate stairs (proximal muscle weakness), a feature of severe rickets which has also been reported by Di somma et al²⁰ as a plausible neurological presentation of rickets. This led to a delay in referral to appropriate clinic, as she was

initially referred to Neurology clinic for a possible Neuromuscular disorder.

Jaja et al²¹ reported that although most of the children with rickets presented with genu valgus or varus deformities, only 35.7% had radiologic confirmation of Rickets. The others may have had healed rickets or other bone abnormalities. UND and UNE both presented with bilateral genu valgus with wind-swept deformity (X-rays showing splaying and fraying of distal femoral and proximal tibial and fibular metaphysis). ELO presented with bilateral genu valgus and widening of both wrists (X-rays showing splaying and cupping of ulnar and radial metaphysis).

Both sets of twins were commenced on Vitamin D and Calcium supplementation and were advised to increase their exposure to sunlight. Evidence is yet to verify what actually constitutes adequate sunlight exposure in children.

For UND and UNE, there was poor compliance to therapy due to financial constraints and possibly ignorance on the part of their mother. Hence, response has been poor. Currently being tracked for further follow-up. On the contrary, ELO has done very well. Her serum calcium levels have normalized after 2 weeks of therapy. Clinically, she is much better as she is now able to move about the staircase without support and is generally more active. She is also being followed up and was billed for repeat X-rays and alkaline phosphatase assay at 3 months after commencement of treatment. But mother is reluctant to repeat investigations because she feels the child is now well.

The diagnosis of renal rickets was ruled out as both sets of twins had normal renal profile and were not anaemic. There was no family history of short stature, orthopaedic anomalies or parental consanguinity, thus making genetically inherited rickets unlikely.

All 3 patients had reduced exposure to sunlight because of COVID-19 pandemic restrictions as well as inadequate dietary intake of calcium and vitamin D especially

with UDE and UNE. The global Consensus Recommendations on Prevention and Management of NR suggests vitamin D supplementation of 400IU(10ug) /day for infants (0-12 months) regardless of mode of feeding; and 600IU(15ug) thereafter, either through diet or supplementation. Supplementation is especially important, in the absence of food fortification, in at risk children, especially in those with a history of VDD, and in pregnant women etc. Specifically asking about sunlight exposure during this peri-pandemic period can help identify those at risk who may require vitamin D supplementation.

The Challenges in low resource settings such as ours include; *late presentation* as seen with UNE and UDE due to ignorance about NR and its features; *delay in diagnosis* - often due to financial constraints in carrying out investigations. Some necessary diagnostic tests are not readily available and are only done reliably in specialist laboratories sometimes entailing shipping the specimen to more technologically advanced nations; *delay in initiation of appropriate treatment* mainly due to financial constraints in purchasing drugs, at exorbitant cost occasioned by the high level of inflation coupled with unavailability of vitamin D capsules which is not produced locally; *Food sources rich in Vitamin D are expensive*: the locally available foods such as eggs, mackerel, crayfish, periwinkles, have become unaffordable to the low income earners or families in the lower socioeconomic class due high level of inflation, as was seen in our patients. Lastly, we had a *high rate of loss to follow up* as seen in UNE and UND who are currently lost to follow-up.

Conclusion: Nutritional rickets among children in Rivers State is on the increase and perhaps is a consequence of COVID-19 pandemic restrictions and worsening nutritional status due to rising inflation in the country. Paediatricians and healthcare workers are hereby alerted to have a heightened index of suspicion to screen and treat nutritional rickets among children with

features of nutritional deficiencies with or without overt bony deformities.

Declaration by Authors

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