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Nutritional Rickets, Mobile Populations and Health Illiteracy: The Experience of a Dedicated Pediatric Bone Center in Greece

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Abstract

Objective: To describe active nutritional rickets in children of mobile populations, assessed in a dedicated, pediatric bone center in Greece.

Methods: Retrospective analysis of demographic, nutritional, clinical, laboratory and imaging data. Evaluation of compliance to follow up advice, as a proxy for health literacy. Comparisons between girls and boys, infants/toddlers vs older children and also between those with vitamin D deficiency (25-OH-D<12 ng/ml) and insufficiency (vitD 12-20 ng/ml). Correlations between different key parameters of nutritional rickets (anthropometry, parathormone, vitamin D, calcium intake, hemoglobin levels).

Results: Thirty-one patients were studied (13 girls, mean age 2.1 years). Their mean daily calcium intake was low (366±172 mg/day) and twenty patients had vitamin D <12 ng/ml. The commonest presenting symptom was delay in walking (29%) and the commonest sign was wrist enlargement (48.4%). Cupping and fraying of the metaphyses were present in 56% of the patients. The patients with short stature tended to be boys, aged <4 years and those with anemia. Significant negative correlations were found between parathormone and daily calcium intake (*r -0.75, p 0.01)*, as well as between PTH and height Z-score (*r -0.51, p 0.03)*. Finally, half of the patients were lost to follow up, whereas only eight families followed the advice for family screening for rickets.

Conclusions: Careful clinical examination and detailed history may reveal the "red flags" and the risk factors for nutritional rickets. Health illiteracy, encountered frequently when treating children of mobile populations, is a challenging issue worldwide and needs further research, to ensure better outcomes.

Keywords: Rickets; Vitamin D; Migrant; Refugee; Bone; Illiteracy; Growth; Nutrition

Introduction

The hope for a better life, natural disasters and war conflicts around the world result in the phenomenon of mobile populations. People belonging to this category are classified either as "migrants" or "refugees", with the main difference being the threat to survival. In other words, refugees are forced to live their home in order to escape from war, violence or persecution, whereas migrants choose to move in quest for work, education or for family reasons [1].

The refugee crisis and migration waves have placed Greece in the eye of the storm. During the last decade, there has been an unprecedented influx of migrants, refugees and asylum seekers. Most of them come from Syria, Iraq and Afghanistan; there are also people from Somalia, Nigeria and Pakistan. Greece has a key

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strategic geographical position, connecting Europe, Asia and Africa. Hence, the national health service is overwhelmed, with thousands of people crossing the borders, aiming to stay in Greece, at least temporarily.

The children of these mobile populations are particularly vulnerable, as they face multiple health risks. They are often malnourished, suffer from infectious diseases and show chronic fatigue [2]. Moreover, these little patients and their families need to navigate into the labyrinth of health service of a developed country, where everything is different; from infrastructure to culture and from language to dietary and health habits of the host nation.

Nutritional rickets (NR), a metabolic bone disorder due to severe vitamin D and/or calcium deficiency, is an entirely preventable condition, characterized by the presence of stunted growth, bone pain, hypotonia, delayed dentition, hypocalcemic seizures, fractures, delay in walking, recurrent respiratory infections or even cardiomyopathy [3]. Clinical signs attributable to NR are craniotabes, bow legs (genu varum), knock knees (genu valgum), rachitic rosary, Harrison's sulcus, wide fontanelles, poor oral hygiene (e.g. enamel defects) and wrist/ankle enlargement [3]. According to the Global Consensus on NR (ref consensus), florid NR is the tip of the iceberg; there are many more cases that are less severe. Nevertheless, active rickets presents with the aforementioned manifestations and is confirmed on X-rays of the wrists and/or the knees, where osteopenia, cupping and fraying of the metaphyses are most commonly seen. The biochemical profile compatible with active rickets shows the pattern of low serum calcium and phosphate levels, high alkaline phosphatase (ALP) and parathormone (PTH), as well as very low levels of 25-OH-D (<12 ng/kg). Values in the range of 12-20 ng/ml are classified as "insufficient", 20-100 ng/kg as "normal" and >100 ng/ml as "toxic" [4].

The aim of this retrospective study is to present the cases of migrant children with severe NR referred to our center during a five-year period. It highlights the clinical, radiological and laboratory manifestations of this rare disorder and also provides an insight of the practicalities of dealing with children and families with poor health literacy.

Patients and Methods

This is a retrospective study of children belonging to mobile populations (migrants or refugees) with nutritional rickets, conducted during the period 2018-2023 at the Department of Bone and Mineral Metabolism of the Institute of Child Health in Athens (ICH), Greece. This department is the only dedicated pediatric bone center in Greece in the public sector. Patients were referred from general pediatricians from all over the country.

Approval of this study was obtained by the Board and the Scientific Committee of the ICH (decision number 91/ date 10/2/2021). Informed consent of the participants and their guardians was not deemed necessary, as there had been no special intervention and data processing served as a departmental audit of clinical practice. All data were retrieved from the patients' medical records and were anonymized during statistical analysis.

Inclusion criteria: Migrant or refugee children (age range 0-18 years) with 25-OH-D levels < 20 ng/ml.

Exclusion criteria: Fracture within six weeks of the clinical assessment, comorbidities or medications affecting bone metabolism (e.g. epilepsy, chronic steroid treatment), treatment with vitamin D and/or calcium supplements at the time of the assessment and diagnosis of genetic rickets.

Communication with the patient and the family during the appointment was possible either through an interpreter or in English or in the presence of a friend or relative able to communicate in Greek or English.

Classification of retrieved data

The collected data were divided into demographic, nutritional, clinical, biochemical and radiological. In terms of health literacy, compliance to follow up appointments, treatment instructions, attendance of other relevant clinics and response to the advice for family screening were evaluated.

Demographics

The following parameters were included: age, gender, country of origin, birthplace, number of years in Greece, history of consanguinity and number of children in the family.

Nutrition

Duration of exclusive breastfeeding, mother and child vitamin D supplementation and daily dietary calcium intake, using an appropriate questionnaire [5] were recorded.

Clinical symptoms and signs

The clinical features studied were: growth (Z-scores for weight, height and body mass index (BMI)) and the presence of bowlegs, knock knees, wrist/ankle enlargement, rachitic rosary, fractures, history of hypocalcemic seizures, cardiomyopathy, recurrent respiratory infections, hypotonia, bone pain, craniotabes and poor oral hygiene (e.g. caries, enamel hypoplasia).

Laboratory indices

The basic bone profile performed in this cohort, included fasting serum for calcium (Ca), phosphate (P), magnesium (Mg), creatinine, albumin, liver function tests, alkaline phosphatase (ALP), parathormone (PTH), 25(OH)D (vitD) and 2nd fasting morning void for Ca, P and creatinine. Moreover, hemoglobin (Hb) and ferritin levels were assessed.

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Table 1: Symptoms and clinical signs of NR in the study population.

Symptom	Absolute number per 31 patients and frequency (%)
Delay at onset of walking (>18 months)	9 (29 %)
Bone pain	3 (9.6 %)
Recurrent respiratory infections	3 (9.6 %)
Fracture	2 (6.4 %)
Hypocalcaemic seizures	1 (3.2%)
Fatigue	1 (3.2%)
Clinical sign	
Wrist/ankle enlargement	15 (48.4%)
Poor dental hygiene	11 (35.5%
Genu varum (bow legs)	10 (32.3%)
Rachitic rosary	6 (19.4%)
Hypotonia	5 (16.1%)
Z-score height < -2	5 (16.1%)
Z-score weight < -2	4 (12.9%)
Z-score BMI <-2	4 (12.9%)
Waddling gait	3 (9.6%)
Genu valgum (knock knees)	2 (6.5%)
Big anterior fontanelle	2 (6.5%)
Scoliosis	2 (6.5%)
Harrison's sulcus	1 (3.2%)
Craniotabes	0
Cardiomyopathy	0

BMI: body mass index, NR: nutritional rickets



Figure 1: Diffuse osteopenia, genu varum, cupping and fraying of the metaphyses of long bones at diagnosis of severe nutritional rickets.



Figure 2: Remarkable improvement at follow up of the same patient, having completed three months of treatment with cholecalciferol and calcium supplements.

Table 2: The key biochemical markers for NR of the study population.

Laboratory parameter	Median value	Minimum value	Maximum value	Reference value
Calcium (mg/dl)	9.2	5.2	10.4	9-11
Phosphate (mg/dl)	4.5	1.7	6.5	4-6
ALP (U/L)	360	130	2426	60-240
uCa/uCreat (mg/mg)	0.07	0.001	0.7	<0.2
25(OH)D (ng/ml)	8.4	3	19	20-100
PTH (pg/ml)	96	34	863	15-60
Hb (g/dl)	12	8.3	15.4	12-15
Ferritin (ng/ml)	32	6	803	15-120

ALP: alkaline phosphatase, PTH: parathormone, uCa: urinary calcium, uCreat: urinary creatinine

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Imaging studies

In the available wrist and/or knee Xrays, the findings that were looked for were: osteopenia, cupping and fraying of the metaphyses and fractures.

Health literacy

Finally, to assess overall communication barriers, the attendance at three-monthly follow up appointments at the ICH was recorded, as well as the outcome, as a proxy for compliance to treatment. In addition, family screening for NR (to an adult endocrinologist for the parents and at the ICH for the siblings) was also offered and the response to this advice was also evaluated. As per protocol, patients were also advised to arrange an appointment with the orthopedic surgeon and the pediatric dentist for longitudinal follow up. These appointments are arranged in different sites, using a phone helpline (national four-digit number), only available in Greek.

Statistics

Regarding statistical analysis, it was performed using IBM SPSS version 29.0. For comparison between different age groups, all anthropometric values (weight, height and BMI) were converted to Z-scores, using the WHO growth charts. Normality of distribution was assessed with Kolmogorov-Smirnov test. Parameters with normal distribution are expressed as mean ± SD (standard deviation), whereas values with skewed distribution are indicated as median and range (minimum, maximum). For comparisons of continuous variables, student's T-test was performed and for categorical ones, the chi-square test. Due to the small sample size, Spearman's correlation between variables was used, with calculation or the index *r* and *p-value.* The level of statistical significance was set at $p< 0.05$.

Results

Study population overview

Thirty-one migrant and refugee patients were referred by other pediatric clinics for a comprehensive assessment of bone health, due to symptoms and signs compatible with NR or because their laboratory and/or imaging tests, requested for other reasons (e.g. respiratory infection), were suggestive of rickets. The patients were assessed throughout the year, during the period 2018-2023.

Demographics

Most of the patients were toddlers, with the median age of the subjects being 2.1 years (range 0.04-14.8 years); there were thirteen females and eighteen males. Most of them (45.2%) came from the Middle East (Syria and Iraq), 25.8% from Asia (Afghanistan and Bangladesh), 19.4% from Africa (Ethiopia, Nigeria, Gambia and Somalia) and 3.2% for other parts of Europe (Romania). Those patients coming from Asia or the Middle East had intermediate skin complexion, as opposed to African patients, who had dark skin. All mothers except for two were veiled, in contrast to their children, who were not.

Greece was the birthplace for 25.8% of the patients, whereas the rest had been born in their country of origin. Five subjects had just arrived in Greece. The remaining twenty-six patients had been living in the country for two to six years.

Regarding family status, there was a history of consanguinity in 28.6%. The number of children per family ranged from one to six, with the majority reporting two (45.2%) or three children (29%). It is worth noting that eight children (26%) were diagnosed with nutritional rickets through family screening.

Nutrition

The duration of exclusive breastfeeding was prolonged, with a mean value of 12.9 ± 5.2 months. The majority of the patients had never been on vitamin D supplements, except for three children, who were taking 400 IU of cholecalciferol for a few months in the past. Of note, the same was true for the respective mothers. Regarding dietary calcium intake, it was equally suboptimal, with a mean value of 366±172 mg/day.

Clinical symptoms and signs

Regarding growth, mean Z-score for weight was -0.5±1.8, Z-score for height was -0.8±1.7 and Z-score for BMI was -0.2±2.7. Table 1 shows the frequency of symptoms and signs of NR in this particular population. Of note, wrist enlargement, poor dental hygiene (e.g. enamel hypoplasia) and genu varum ("bow legs") were the commonest signs, whereas delay in walking was the most frequent symptom reported, followed by bone pain and history or recurrent respiratory infections.

Laboratory indices

Overall, twenty out of thirty-one patients (64.5%) were found vitamin D deficient (<12 ng/ml) after a routine laboratory work up, with the rest having vitamin D 12-19 ng/ml (insufficiency). Table 2 provides an overview of the key diagnostic markers for NR. The indices not shown were within normal limits (i.e. Mg, creatinine, albumin, liver function tests, urinary phosphate and creatinine).

Imaging studies

The X-rays performed for confirmation of NR were reported as normal in only two patients (6.5%). Further review of the images revealed osteopenia. This was a universal finding, either in isolation (nine patients, 30% of the study population), or combined with the cupping and fraying of the metaphyses at the X-ray or the wrist and/or the knee. These findings are the main radiological features of NR and their frequency was 56% (seventeen patients). On one occasion, a post traumatic fracture of the radial metaphysis was noted in

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an adolescent. Rachitic rosary was diagnosed radiologically (chest X-ray) in one patient. Interestingly, severe osteopenia was recorded as a random finding in X-rays that were performed for other indications (e.g. injury, respiratory infection) and prompted further referral to our center for bone health assessment in eleven patients (35.5%). Figure 1 shows active nutritional rickets in an African toddler and his remarkable radiological improvement under treatment after three months (Figure 2).

Health illiteracy

Nearly half of the patients were lost to follow up (sixteen patients, 51.6%). Although they were given instructions for treatment with therapeutic doses of cholecalciferol (depending on age) and calcium supplement, they did not show up three months later for re-evaluation. Despite active efforts to communicate with them, their contact details proved inaccurate or had changed or they had moved to different parts of the country or abroad without informing the department.

Of the remaining fifteen patients, eleven presented with healing of rickets (normal laboratory indices and X-ray) and four with considerable improvement, with two of them having persistent genu varum for a year. Screening of the siblings for NR was performed only in eight families, whereas the number of the parents who were assessed for NR is not clear. Moreover, the exact number of patients who actually visited the orthopedic surgeon and/or the dentist is also unknown.

Comparisons between different groups

As a first step, growth parameters of the children with NR (i.e. Z-scores for weight, height and BMI) were compared to the general population, assuming that the 50th centile for weight, height and BMI corresponds to Z-score=0. Only Z-score for height was found significantly lower (p= 0.04), whereas the difference in weight and BMI did not reach statistical significance.

When anthropometric values were compared in terms of gender, males were found shorter than females (Z-score for height -1.4±1.8 vs 0±1.1, respectively, p=0.04), whereas they did not differ significantly in weight and BMI.

When infants and toddlers (age < 4 years) were examined as a separate subgroup from the older children (≥ 4 years), the former were found shorter, whereas weight and BMI were comparable. However, this difference in height Z-scores did not reach statistical significance (-1.3±2.1 vs -0.4±1.2, p=0.2).

Comparisons between different areas of origin (i.e. Africa, Asia and the Middle East) were not attempted, due to the small number of patients per category.

As far as the presence of anemia was concerned, the group with hemoglobin <12 g/dl had lower Z-scores for weight (-1.6 ± 1.7) and height (-2.64 ± 2.1), compared to the patients with higher hemoglobin values (-0.3 ± 2 and -0.2 ± 1.3, respectively). The differences observed were not statistically significant.

Finally, the study population was divided between those with vitamin D deficiency (25-OH-D<12 ng/ml) and those with insufficiency (25-OH-D= 12-20 ng/ml) and further comparisons were performed. These are illustrated in Table 3. Of note, none of the reported differences between the groups reached statistical significance.

Table 3: Comparison of key parameters between patients with vitamin D deficiency vs insufficiency.

Parameter	25(OH)D (ng/ml)	Mean value± SD
Age (years)	≥ 12-20	2.9±2.3
	<12	5.3 ± 4.7
Calcium intake (mg/day)	≥ 12-20	433 ± 135
	<12	335 ± 219
ALP (U/L)	≥ 12-20	416 ± 323
	<12	867 ± 840
Z-score weight	≥ 12-20	-0.3 ± 1.2
	<12	-0.7 ± 2.4
Z-score height	≥ 12-20	-0.3 ± 1.5
	<12	-1.4 ± 1.9
Z-score BMI	≥ 12-20	0.3 ± 0.8
	<12	-0.5 ± 4.2

ALP: alkaline phosphatase, BMI: body mass index, SD: standard deviation

Correlations between different key features of NR

Correlations were explored between the variables: Vitamin D, age, growth Z-scores (weight, height and BMI), laboratory values (ALP and PTH), daily dietary calcium intake and hemoglobin levels. As expected, age and weight are positively correlated with height, whereas PTH is negatively related to height and calcium intake. Of note, hemoglobin levels show positive correlation with anthropometric values, possibly reflecting adequate nutritional status. Table 4 presents only those correlations with statistical significance, along with the respective *r* and *p* values.

Table 4: Correlations between different NR parameters.

Parameter 1	Parameter 2	Correlation coefficient (r)	p-value
Age (years)	Z-score Ht	0.41	0.05
Z-score Wt	Z-score Ht	0.68	0.001
	Z-score BMI	0.86	0.001
	Hemoglobin	0.45	0.04
Z-score Ht	Parathormone	-0.51	0.03
	Hemoglobin	0.58	0.01
PTH	Daily Ca intake	-0.75	0.01

Wt: weight, Ht: height, BMI: body mass index, PTH: parathormone

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Discussion

According to a report of the European Union on the migratory crisis, the influx of mobile populations has been unprecedented, with nearly 1.5 million people arriving in the continent in 2015 [6]. Another interesting statistic is the percentage of mothers who are first-generation migrants and give birth in Europe; it is estimated at over 20% [7]. Given that migrants and refugees are at high risk for nutritional rickets, due to their cultural differences (e.g. skin coverage), skin complexion and dietary habits (e.g. low vitamin D or calcium intake, malnutrition), it is not surprising that the reported prevalence of this entirely preventable and treatable metabolic bone disease is rising in developed countries (60–2,300 per 100,000) [8]. As a result, various national and global guidelines are in place, in order to tackle this issue [2,4].

This study aimed to describe the holistic assessment of pediatric patients with active rickets in a dedicated pediatric bone center. They had a mixed migratory status (refugees and migrants) and were also heterogeneous in terms of country of origin and number of years in the host country. Most of them were infants and toddlers; this was not surprising, given the high growth velocity, the increased nutritional requirements and the more striking manifestations of NR at this age [9,10]. Moreover, nearly all mothers were veiled and on no vitamin D supplements, placing their offspring (and themselves) at risk for rickets from an early age.

There was no gender predilection for NR in our cohort; this is probably due to the small number of patients of the study group. According to other studies, girls are more frequently and more severely affected, because of the practice of veiling and also their tendency to stay indoors [8,11,12]. Of note, consanguinity was noted in nearly one to four families and this is in accordance to other works [13]; this information is important, as there is always the possibility of NR coexisting with genetic rickets or another inherited bone disorder, in which case more diagnostic tests and different treatments should be offered.

Regarding the patients' dietary habits and nutritional profile, prolonged (> six months) exclusive breastfeeding and lack of maternal vitamin D supplementation during pregnancy were noted in most cases; these are well established predisposing factors for NR [14]. In addition, their calcium intake was poor, with the lowest levels reported in those with severe vitamin D deficiency. In fact, a negative correlation was found between PTH levels (a marker of NR severity) and calcium intake. According to the global consensus on NR, dietary calcium intake < 300 mg/day increases the risk of NR, regardless of vitamin D levels [4].

To our knowledge, this is the only study which ranks the clinical signs and symptoms in terms of frequency, providing useful "red flags" for NR diagnostic work up. In this cohort, delay in walking was the most frequent complaint, followed by bone pain and recurrent respiratory infections. Consequently, a high index of suspicion for NR should be present in these scenarios. As far as the clinical signs are concerned, enlarged wrists, dental defects and bow legs were the commonest; these are easy to detect during a routine clinical examination and have also been described elsewhere [2,9]. Of note, the inspection of the teeth by the pediatrician as a means of suspecting rickets has never been described to date, although it can be performed easily and can be very informative [15].

In this cohort, short stature was also an important feature, especially in boys, small children (< 4 years old) and those with anemia. Iron deficiency possibly reflects malnutrition (hemoglobin levels showed positive and statistically significant correlations with weight and height Z-scores) and may also adversely affect vitamin D handling in the gut, the skin or other stages of its metabolism [12]. Compromised growth is also reported by others [3,16].

The fact that low vitamin D levels (< 20 ng/ml) were detected in most cases randomly (opportunistic approach in high risk populations), during a pediatric check up, is noteworthy. The European Academy of Pediatrics advises that vitamin D should be part of a battery of tests performed on arrival of migrant/refugee children in the host country [2]. The biochemical hallmark of active rickets is the combination of vitamin D deficiency (25-OH-D < 12 ng/ml) with very high ALP and PTH values, as also described by Kurnaz et al. [17]. Moreover, a negative correlation was found between PTH and height, reflecting the severity of NR and its effect on longitudinal growth. Lack of vitamin D rarely occurs in isolation; other micronutrients may also be deficient, e.g. zinc and iron [3].

Most of the patients had characteristic rachitic changes on their X-rays. The severity and duration of NR dictates the presence of key findings [18]. Initially, only osteopenia is detected, followed by cupping and fraying of the metaphyses at a later stage [3]. It is worth searching for the above findings in every child at risk of NR in any X-ray, regardless of the indication, in order not to miss the diagnosis, as it was evident from the results of this study and this is an important learning point. Only one fracture was detected. As this is more frequent in adolescents [19] and most of our patients were younger, this could be a plausible explanation.

The compliance of the families to the proposed treatment, family screening for NR, follow up and the attendance of appointments with other colleagues (e.g. the orthopedic surgeon) served as indicators of health literacy. According to Sørensen et al. [20], "health literacy incorporates the knowledge, motivation and competences to access, understand, appraise and apply health information in

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order to make judgments and take decisions in everyday life concerning health care, disease prevention and health promotion to maintain or improve quality of life throughout the course of life".

In this study, half of the patients were lost to follow up and this is comparable to existing literature data [13]. The patients who attended their follow up appointments had a good outcome. In terms of the advice for family screening for NR, 26% showed up; in addition, it is unknown whether the patients attended other clinics for further assessment. This profile reflects a status of "health illiteracy" of the migrant/refugee families and also the lack of readiness of the national health systems to respond to acute and increasing demands for patient care. Following these observations, local policy has been modified and we now suggest Stoss therapy under certain circumstances and also hospital admission in selected cases, where there is urgent need to assess for acute complications (e.g. hypocalcemic seizures, cardiomyopathy etc.). These practices are also common in other countries [13,21,22].

The causes of health illiteracy are multiple and global. In fact, there are too many barriers to proper navigation of the families in the complex health systems of the developed countries. On the one hand, mobile populations have different culture and language. They often have many children in the household, they face financial hardship, frequent changes of address, social stigma and uncertainty for the future [23]. Their perception of health risks and also their feeding practices may be different from those of the Western world. They might as well feel embarrassed to show that they do not understand or have fears of discrimination [22]. On the other hand, national health systems are overwhelmed; their preparedness to provide health services to these populations is suboptimal and the patient's orientation in a complex system can be a challenge [24]. Interpreters are not always available and communication can be very problematic. Moreover, nursing and administrative staff is usually not enough to help the families to move through the system, ensuring attendance to appointments and compliance to further referrals [23].

So, what needs to be done to address this phenomenon of health illiteracy? There are inspiring initiatives which show the way forward. For example, Somalian families got help in a USA state by a stepwise approach, including the distribution of informative leaflets in Somalian, the provision of free vitamin D supplements and proper counseling on the benefits of vitamin D supplementation [25]. A more sophisticated approach is followed in Sweden, where mobile health (mHealth) interventions are in place, appropriately tailored to the migrants' needs. More specifically, a mHealth application is delivered to migrant women after childbirth, with useful lifestyle advice (diet and exercise) and also health literacy information (i.e. function of healthcare system, access to suitable sources of health information and patients' rights). Of note, this software is available in four languages and it can provide both text and audio materials [7]. The final goal is to empower the families, in order to achieve better health outcomes [26]. In addition, community health workers may promote prevention of NR and bridge the gap between the families and the health care system, facilitating communication and ensuring better outcomes [23].

This study has certain strengths and limitations. On the one hand, given the rarity of NR, it provides comprehensive data in a holistic way, in order to familiarize every pediatrician with the disorder, especially in view of the rising number of migrants and refugees worldwide. It also offers insight on the challenging practicalities of everyday practice, with regards to health illiteracy, in an effort to abolish the communication barriers and improve outcome. On the other hand, the study population is small and the data were collected retrospectively, with no reference on their seasonality. Nevertheless, the importance of addressing the public health issue of nutritional rickets is undoubtful.

In conclusion, the severe cases of NR presented in this study describe the "tip of the iceberg", as milder cases may go unnoticed. It highlights the systematic diagnostic approach and the usual "red flags" for early suspicion of the disorder and-most importantly-the practicalities and challenges regarding compliance and long-term outcomes. Public health policies should be in place to prevent NR rather than treat it and this is a demanding, but achievable goal, which necessitates the cooperation of all healthcare stakeholders.

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Conflict of Interest Statement

The author declares no conflict of interest.

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