

Evaluation of Rickets in a Developing Country: Presentation and Risk Factors

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ABSTRACT

Background: Rickets is a preventable mixed group of acquired and inherited diseases causing disturbances in calcium and/or phosphate homeostasis that affect the growing skeleton disease of growing children and adolescents, leading to the softening and weakening of bones. This study aims to describe the presentation of Rickets in children attending a tertiary hospital in a developing tropical country.

Methods and Materials: The study design is cross-sectional and hospital-based. The study data was collected from hospital records and utilized clinical history, clinical examination, and results of laboratory investigations. The collected data was analyzed by SPSS v27.

Results: The mean age of the rickets children included in the study was (22.3 ± 15.1 months). Male (55.4%) children are more present than females (44.6%). About 80.4% (45) of the children were from families with low socioeconomic status. Most children's fathers (53.6%) have a good educational background compared to their mothers (44.7%). Children who received breastfeeding accounted for 42 (75%), while those who did not breastfeed accounted for 14 (25%). Most children are exposed to sunlight less (73.2%). The majority (92.9%) of children were underweight. Male (55.4%) children are affected more than females (44.6%). Rachitic rosary (75%) and wrist swelling (69.6%) are the most common manifestations. About 92.9% of screened children had both hypocalcemia and hypophosphatemia. The alkaline phosphatase enzyme increased 91% (51) of the studied cases.

Conclusion: Low socioeconomic status, low exposure to sunlight, and mothers' educational background were essential in developing Rickets among the studied children. Rickets affected Male children more than females, and Rachitic rosary and wrist swelling are the most common manifestations. Most of the children showed positive laboratory findings.

Keywords: Rickets; Socioeconomic Status; Rachitic Rosary; Breastfeeding; Children.

INTRODUCTION

Rickets is a preventable disease of growing children and adolescents^{1,2}. Rickets is a mixed group of acquired and inherited diseases causing disturbances in calcium and/or phosphate homeostasis that affect the growing skeleton³. Although Rickets have been known since the mid-seventeenth century, they are still considered a frequent disease (4). The occurrence of Rickets has noticeably declined compared with the prevalence in the past, but the disease has re-emerged in both developed and developing countries^{4,6}.

Rickets is categorized into two major groups: (a) calcipenic due to inadequate calcium intake, Vitamin D deficiency, the defective metabolic pathway of Vitamin D or resistance of the target tissues to calcitriol, (b) phosphatopenic due to deficient intake, impaired intestinal absorption or increased renal loss of phosphorus.⁷ Also, Rickets is subdivided into three subtypes⁸: Hypophosphatemic rickets, which is vitamin-D-resistant, develops secondary to renal phosphate wasting. Vitamin D-dependent rickets (defects of vitamin D metabolism). Nutritional Rickets (caused by dietary deficiency of vitamin D, and/or calcium, and/or phosphate).

Although nutritional Rickets are more common in low- middle-income countries, they remain the most common globally. Most Rickets manifest as bone deformities, bone pain, and impaired growth velocity. Diagnosis of Rickets is established through medical history, physical examination, biochemical tests, and radiographs. It is of crucial importance to determine the cause of Rickets, including the molecular characterization in the case of vitamin D-resistant rickets, and rapidly initiate the appropriate therapy^{2,9,10}.

The primary pathogenesis of Rickets is under-mineralizing the growing cartilage, caused by disordered chondrocytes' differentiation and maturation resulting from abnormal levels of serum calcium and phosphate, leading to bowing and swelling of bone, particularly long ones.^{1,2,8,11,12}

The parathyroid–bone axis is responsible for preserving blood calcium levels and is activated by low intestinal calcium absorption. The activated parathyroid–bone axis increases bone resorption and decreases calcium renal loss, reducing tubular phosphate resorption, which manifests as hypophosphatemia¹³

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The general character of Rickets is impaired apoptosis of the growth plate's hypertrophic chondrocytes resulting from hypophosphatemia. This leads to the widening of the growth plates of growing bones, which is frequently associated with osteomalacia^{3,14}. The denominator of all types of Rickets is hypophosphatemia, except in the case of metabolic acidosis and CKD-associated Rickets, and is responsible for developing the clinical and radiological manifestations of rickets^{3,12}.

Ricket can be due to the absence of direct exposure to sunlight or skin problems¹⁵⁻¹⁷. In contrast, nutritional Rickets develop due to a lower intake of minerals or calcium or phosphorous deficiency¹⁸. The etiology of calcium deficiency is related to insufficient intake or intestinal problems, while phosphorous deficiency is linked to renal and endocrine problems¹⁸. Vitamin D deficiency can cause Rickets, bone problems, physical growth failure, and defects in motor development¹⁵. Scientific evidence supports that vitamin D deficiency in infancy can be a predisposing factor for some diseases, such as diabetes mellitus, cancer, and multiple sclerosis². The different causes and etiologies of Rickets spread the occurrence of Rickets in developing and developed countries^{10,12}. In developing countries, nutritional Rickets are the main type¹². Other etiologies of Rickets such as less exposure to sunlight. Skin problems, insensitivity to vitamin D, dietary calcium deficiency due to cultural practices, hereditary and intestinal problems can be present in both developed and developing countries^{10,19,20}.

This study aims to describe the presentation of Rickets in children in a tertiary hospital in a developing country.

METHODOLOGY

The study design is cross-sectional and hospital-based²¹. The sampling technique covers all children referred to or presented to the emergency department of Jafar Ibn Auf Pediatric Hospital in Khartoum, Sudan, from June 2019 to June 2021. The inclusion criteria were any child referred to or presented to the emergency department with features suggesting or clinical signs of Rickets was included in the study. The exclusion criteria are non-Sudanese or aged more than 15 years. The total number of the included children was 56.

Data collection

Data was collected from all the included children through two methods. The first method was an epidemiological questionnaire, and the second was a clinical workup. The epidemiological questionnaire assessed all family data, including socioeconomic status, living conditions, parental education, nutritional data, milk and dietary calcium and supplementation, and sunlight exposure. The clinical workup and the diagnostic criteria for Rickets were seated according to WHO Child Growth Standards (2007), Levine (2020), and Haffner et al. (2022)^{3,22,23}. The investigations include a complete blood count, renal function test, liver function test, serum calcium, serum phosphorus, serum alkaline phosphatase, and X-ray^{19,20}.

Ethical consideration

The study was conducted in compliance with the Declaration of Helsinki and approved by the ethical and research committee of Jafar Ibn Auf Pediatric Hospital (Khartoum, Sudan). Informed written consent was obtained from the children's parents after they had agreed to participate.

Statistical analysis

The obtained data were tabulated in an Excel sheet and analyzed by SPSS v27. The categorical data were presented in the form of tables and frequencies.

RESULTS

The study group's ages ranged from 8 to 59 months; the mean was 22.3±15.1 months. Male children represent 55.4%, while females were 44.6%. About 80.4% (45) of the children were from families with low socioeconomic status, while 19.6% (11) were from moderate socioeconomic status (Table 1).

Most of the children's fathers have a good educational background (53.6% university level and 25% secondary school). In contrast, less than half (44.7) of mothers reached secondary school, and only 32.1% have a university degree.

Children who received breastfeeding and developed Rickets were 42 (75%), while those who didn't receive breastfeeding were 14 (25%). Children with adequate sunlight exposure per day were 15 (26.8%), while those with under-exposure were 41 (73.2%). The majority of children were underweight (92.9%) (52), and those with normal weight were only 4 (7.1%) Table (1).

Table 1. Show sociodemographic data of rickets children who attended Jafar Ibn Auf pediatric hospital, Khartoum, Sudan, from June 2019 to June 2021 (N=56).

General characteristics		Frequency	Percentage
Gender of the children	Males	31	55.4
	Females	25	44.6
Socioeconomic status of the family	Low income	45	80.4
	Moderate income	11	19.6
	High income	00	00
Father Educational level	Primary school	12	21.4
	Secondary school	14	25
	University	30	53.6
Mother Educational level	Primary school	13	23.2
	Secondary school	25	44.7
Breastfeeding	University	18	32.1
	Yes	42	75
Enough exposure to sunlight	No	14	25
	Yes	15	26.8
Weight of the child	No	41	73.2
	Underweight	52	92.9
Others	Normal weight	4	7.1
	Liver failure	6	10.7
	Renal failure	8	14.3
	No complications	42	75

The laboratory findings of the screened children show that 92.9% (52) had hypocalcemia and hypophosphatemia. The levels of alkaline phosphatase enzyme were increased in 91% (51) of the subjects (Table 2). The precipitating factors for Rickets were liver failure at 11.1% (6) and renal failure at 14.8% (8).

Table 2. Show the laboratory findings of rickets children who attended Jafar Ibn Auf pediatric hospital, Khartoum, Sudan in the duration from June 2019 to June 2021 (N=56)

Laboratory findings		Frequency	Percentage (%)
Serum calcium	Hypocalcemia	52	92.9
	Normal	4	7.1
Serum phosphates	Hypophosphatemia	52	92.9
	Normal	4	7.1
Serum alkaline phosphatase	Increased	51	91
	Normal	5	9

Table 3. Show the frequency of Clinical signs seen among rickets children who attended Jafar Ibn Auf pediatric hospital, Khartoum, Sudan duration from June 2019 to June 2021 (N=56)

Clinical symptoms		Total number		Gender distribution		
		Frequency	Percentage	Gender	Frequency	Percentage
Rachitic rosary	Yes	42	75	Males	23	54.8
	No	14	25	Females	19	45.2
Hands swelling	Yes	39	69.6	-	-	-
	No	17	30.4	Males	21	53.8
				Females	18	46.2
				-	-	-

The common clinical presentation among studied children was a rachitic rosary 42 (75%), followed by hand swelling 39 (69.6%) (Table 3). Rachitic rosary and hand swelling were more common among males, 23 (54.8%) and 21 (53.8%), respectively, than among female children, 19 (45.2%) and 18 (46.2%).

DISCUSSION

This study describes the presentation of Rickets among children who attended Jafar Ibn Auf pediatric hospital in Khartoum, Sudan, from June 2009 to June 2011. Many reports claimed that non-Caucasian ethnic groups in general and Middle Eastern and Sub-Saharan in particular are at high risk of developing nutritional rickets^{5,15,24-27}. Both Callaghan et al. and Munns et al. reported an increased incidence of Rickets among African and Asian children below five years of age, even though they were in European countries^{5,15}. They have related such findings to skin pigmentation and the wearing of clothes that cover most of the body, hence decreasing exposure to sunlight and consequently reducing the production of biologically active vitamin D. In addition to that, lack of supplementation and prolonged, exclusive breastfeeding can contribute in the development of Rickets among children²⁷.

The mean age of the studied children was 22.3±15.1 months, similar to previous studies by Flot C et al. 2020 and Robinson PD et al.²⁸⁻³⁰. Flot C et al. 2020 (22) reported that most of the diagnosed cases were seen in early childhood and adolescence and were associated with symptoms of hypocalcemia.

In this current study, male children are more affected (55.4%) than females (44.6%). This finding is consistent with the literature where it is reported that male children are more affected^{22,25,26}. Genetic or social-cultural factors were suggested to explain the predominant affection of male children^{28,30,31}. Genetic factors may include high calcium requirements due to males' higher bone mineral content. Social-cultural factors include that males are commonly breastfed longer and wear a veil. Social-cultural factors include the fact that males are commonly breastfed longer and don't wear a veil.^{24,30,32}

In the current study, the majority of studied rickety children had breastfed (75%) but had no adequate exposure to sunlight (73.2%) and were underweight (92.9%). These findings agree with Gartner et al. (2003) and Özkan (2010). They reported that breastfeeding without supplementary vitamin D or inadequate sunlight exposure can increase the risk of developing vitamin D deficiency or Rickets. Decreased sunlight exposure can be due to cultural habits or seasons^{2,33}. Chanchlani et al. (2020) reported in the presence of adequate exposure to sunlight, the cause of Rickets can be local community culture or custom, such as the widespread practice of a vegetarian-based diet³⁴.

In the current study, the educational level of most of the included children's mothers is poor. Of those in secondary school, 44.7% and

primary school 23.3%), the father's educational level is far better than the university level (53.6%). Ejaz et al., 2013 reported that a high level of parental education minimized the risk of Rickets among children¹ while Craviari et al. 2008 reported that a high incidence of Rickets is associated with low maternal education³². Mothers' educational background can affect children's nutritional status through a lack of information regarding the importance of breastfeeding and supplementary food intake for their children. Another factor influencing children's nutrition is the family's socioeconomic status and large family size. The majority of the families of the included children have low socioeconomic status. Many studies in developing and developed countries supported the association between poor nutrition and low socioeconomic status with the risk of developing rickets^{1,32,35,36}. Low Nutritional status can lead to decreased immunity, vulnerability to infection, decreased appetite, and further nutritional deficiencies.³⁷⁻⁴⁰. In contrast, in the USA, inadequate vitamin D intake and reduced exposure to sunlight were reported to cause Rickets among infants³³.

About 14.3% (6) of the studied children were presented with renal failure, identified as renal Rickets. Chronic renal diseases can result in a deficit in the enzyme 1 alpha-hydroxylase, which consequently decreases the production of 1,25 hydroxy vitamin D (calcitriol)³⁴. The most characteristic laboratory finding in such cases is the elevated phosphate level⁴¹.

The laboratory findings showed hypocalcemia and hypophosphatemia among almost all the studied children (92.9% each). Despite the majority of cases having hypocalcemia (92.9%), none of them presented with hypocalcemic seizures. This is controversial to what was reported by previous studies that seizures were the presentation in about 12–25% of children with nutritional rickets^{28,29,31}. Hypocalcemic seizures were reported mainly among those who are less than 12 months, non-Caucasian, and who were breastfed entirely^{28,31}.

The most common clinical symptom among children in the current study is rachitic rosary (75%), followed by hand swelling (69.6%). In both situations, male children are more affected. These findings are supported by previous work of Ozkan et al. (2009) and Ozkan et al. (2010)^{2,9}. Who reported rachitic rosary as the most frequent clinical sign, followed by wide wrist and ankle regions swelling, then posing of the skull and wide anterior fontanel^{42,43}. Skeletal deformities are reported as the symbol of rickets^{4,28}. Their appearance is predominantly before 18 months and depends on the child's weight-bearing patterns of the limbs^{4,8}.

CONCLUSION

The mean age of the presented children was 22.3±15.1 months. Male children were more affected by Rickets. In most cases, the mother's education is low. Hypocalcemia, hypophosphatemia, increased serum alkaline phosphatase, rickety rosary, and hand swelling are the main symptoms.

Limitation and Weakness

The descriptive study design and relatively small sample size are major weaknesses in this study. One nationality was included in the study (racial group), and the mode and duration of sun exposure were not assessed to discover environmental factors that may lead to or aggravate Rickett. The generalizability of the results is impractical as there is no data about the size of the whole population of Ricketts.

Strength

This study forms a baseline study. To some extent, the study provided reliable data about rickets presentations and the associated risk factors.

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