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Research Article

FREQUENCY OF NUTRITIONAL RICKETS AMONG SUSPECTED RICKETS CASES IN DHAKA SHISHU (CHILDREN) HOSPITAL, SHER-E-BANGLA NAGAR, DHAKA

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ABSTRACT

Background: Nutritional rickets (NR) is one of the common form of growing bone disease resulting significant disability unless treated properly. Despite scope of adequate sunlight exposure, which is a source of vitamin D in young child in Bangladesh, increased trend of NR is observed. Considering this fact, the study was designed to explore the frequency of nutritional rickets among suspected rickets cases.

Materials and Methods: The prospective cross-sectional study was conducted in Dhaka Sishu Hospital (DSH) in Bangladesh over a period of 2 years. Child aged 1-5 years attending in DSH with complaints bowing of leg and/or clinical symptoms consistent with rickets were approached. Suspected rickets cases were investigated further and total 100 cases were analyzed. Informed consent and ethical measures were ensured in each cases. Data analysis was done by SPSS 23.

Results: Among the 100 suspected rickets child, mean age was 29.36±13.09 SD (months). There were 64% (n=64) male and rest of them (36%, n=36) were female. Of all, the frequency of rickets was 90%, wherein the frequency of nutritional rickets was 87.78% (n=79). Male sex is associated with higher proportion of NR than female child. Limb deformity is the most common features in group of child and bowing leg, swelling and widening of wrist, rickety rosary and knock knee were present in 51.9%, 27.8%, 26.6% and 25.3% children respectively. Whereas, delayed growth and delayed dentition were present in 26.6% and 21.5% respectively.

Conclusion: Nutritional rickets is the commonest subtype of rickets in Bangladesh.

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INTRODUCTION

Background

Nutritional rickets (NR), a skeletal disease[1],is a global public health challenge resulting significant morbidity and physical disability of the children.[2,3]It usually associated with bone pain and long bone deformities along with enlargement of the wrist and costochondral junctions. Beside these, serious consequences such as, delayed development, linear growth impairment, permanent skeletal malformation, hypocalcaemic seizures, heart failure, and even death can occur also.[1,2,4] Increased prevalence of NR is noticed in developing countries (ranged from 10-70%) particularly where malnutrition is predominate phenomenon.[2,5,6] For last two decades, rickets has become a health concern for Bangladesh and burden with about 8% of affected child.[7] Although both male and female are equally affected, rachitic deformities are more common among boys in this country.[5] Most children with rickets develop symptoms within the first 6-12 months of age but in tropical areas where sunlight is ample, like Asia and Africa, it classically manifests during the second or the third year of life.[8] Vitamin D deficiency seems to be the key component of causing nutritional rickets in many countries of the world.[2,9,10] But inadequate calcium has also been demonstrated as the main etiological factor of children having rickets in several countries[2,3,11] Inadequate ultraviolet light exposure, due to

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avoidance of sun light for conservative maternal clothing culture (such as, veiling), long term breast feeding without taking vitamin D fortified food, reduced intake of milk and dairy products were hypothesized as a reason of this condition. All of these result in inadequate calcium causing impaired skeletal mineralization, which is the underlying pathology of nutritional rickets.[1,12,13]Deficiency of both calcium (Ca) and vitamin D are prevalent in Bangladesh, which is mostly due to poor socioeconomic condition of the people.[7]Although geographical location favors optimum sun-exposure in this areas still vitamin D deficient rickets is prevalent in this region. Along with other factors higher air pollution is seems to be contributing vitamin D deficiency in our country.[7] However, lack of dietary calcium also is believed to be another causal factor of nutritional rickets in Bangladesh.[14]

In past few decades, several study was reported about the devastating effect rickets on children.[3,10,11,12] and revealed the higher incidence of recurrent pneumonia in this group of children.[15] which is a major cause of childhood mortality.[16] As a result, developing countries are facing of double burden of this disease itself and by its complicaitons.[16-18] Nevertheless, it is a matter of hope that confirm diagnosis of active rickets can be made easily with simple investigations such as radiograph and alkaline phosphatase besides clinical examination.[19] Several intervention was practiced to prevent this disease particularly NR. Vitamin D supplementation or by food fortification has proven its efficacy and safe to prevent this disease.[18-20]Moreover, it would be beneficial to prevent early than treatment in context of outcome and expense.[1,5]In context of fewer evidence in NR incidence and prevalence, the study was designed to assess the frequency of nutritional rickets among suspected rickets cases in DSH, Bangladesh.

MATERIALS AND METHODS

Design, subjects and Statistics

All child aged 1-5 years of age admitted to the pediatric ward at Dhaka Shishu Hospital for the first time between August 2015 to July 2017 were included in this prospective cross-sectional study. Child admitted in this hospital with complaints of bow of leg or rachitic rosary chest or any other features consistent with rickets (clinically) were approached for inclusion of the study. Next, biochemical and radiological investigations were done to establish rickets among clinically suspected Childs. Then, serum 25-hydroxyvitamin D (25(OH)D) level was done to identify the stratification of rickets. The diagnosis was validated upon predefined diagnostic criteria; cases fulfilling both biochemical inclusion criteria and clinical signs/symptoms or radiological signs of rickets were included. The diagnosis of rickets was made based on raised plasma alkaline phosphatase (ALP), raised serum parathyroid hormone (PTH), or low/normal serum calcium (Ca) in clinically and radiologically consistent cases.[4,21] Whereas, the diagnosis of nutritional rickets is made on the basis of history, physical examination, radiographs and biochemical testing particularly serum 25(OH)D.[4] The cut off value of Vitamin D deficiency was set as <30nmon/l. To evaluate the other causes of rickets were done according to the standard guidelines.[4]To verify the diagnosis of rickets and its etiology (nutritional, hereditary rickets, and secondary rickets), the entire medical record(s) were carefully reviewed by the investigator. Borderline result was considered criteria of exclusion and it was replaced by another consecutive purposive sampling. The child were divided into three subtypes: nutritional rickets (rickets with vitamin D deficiency), non-nutritional rickets (rickets not due to the deficiency of vitamin D or rickets due to other cause) and rickets like disease (clinically alike to rickets but not proved by investigations). In this study, ethical issues were maintained according to the Helsinki declaration and ensured that parents were not get any financial benefits from this study. Clinical presentation, biochemical and radiological reports were collected and kept recorded in separate case record form. Following, collection of all the required data, these were checked, and tabulated into the computer using the SPSS/PC software 23. The study conducted with 95% confidence level at 5% acceptable error level and p value <.05 was considered as statistically significant.

RESULTS

A total of 100 clinically consistent cases of rickets were evaluated and frequency of nutritional rickets was identified in this study. Total 11 cases were excluded from the study due to unwillingness to bear the investigation expenditure and the same number of study samples was replaced later. Mean age of the children was 29.36±13.09SD (months) with 64% male & 36% female representation.

Diagnosis of rickets was made based on X-ray findings as well as serum alkaline phosphatase level. Of all suspected cases, 90 were confirmed to have rickets and 79 were identified as nutritional deficiency rickets based on 25-hydroxy vitamin D level (Figure 1).

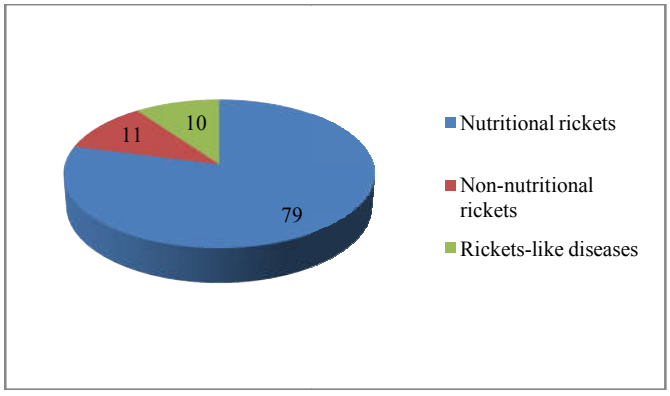

Figure 1 Diagnosis of suspected rickets children (n=100)

Comparative analysis showed that, median serum 25-hydroxy vitamin D was significantly lower in patients with nutritional rickets (median, 21 nmol/L; range, 9-29 nmol/L) than that of children with non-nutritional rickets (median, 66 nmol/L; range, 56 – 90 nmol/L) (p<0.001). Whereas, alkaline phosphatase level was also significantly higher in nutritional rickets group (p value <0.05). Biochemical comparisons are outlined in table 1.

Table 2 shows the detailed biochemistry in children with nutritional rickets. Besides lower 25-hydroxyvitamin D level and increased S. alkaline phosphatase level than reference range, lower serum calcium and serum phosphate level in 36% and 34% cases of nutritional cases. While parathyroid hormone level was high (>7.5 pmol/L) in 81% of nutritional rickets children.

Table 1 Biochemical parameters of Nutritional rickets (n=79) and Non-nutritional rickets (n=11)

Variable	Nutritional rickets Median (Range)	Non-nutritional rickets Median (Range)	*p* value*
25-hydroxyvitamin D nmol/L	21 (9 – 29)	66 (56 – 90)	<0.001
Alkaline phosphatase, IU/L	985 (265 – 4350)	390 (200 – 2010)	0.03
Calcium, mmol/L	2.20 (1.28 – 2.10)	2.30 (2.10 – 2.50)	0.37
Serum phosphate, mmol/L	0.83 (0.12 – 1.39)	0.71 (0.43 – 1.32)	0.99
Parathyroid hormone, pmol/L	9.6 (5.80 – 20.58)	09.50 (6.74 – 14.42)	0.18

* *p* value determined by Mann-Whitney U test

Table 2 Biochemistry of children with nutritional rickets (n=79)

Variable	Normal Range	Median (Range)	Values above or below cut-off point, n (%)	
25-hydroxyvitamin D nmol/L	Sufficient: >50 Insufficient: 30 - 50 Deficient: <30	21 (9 – 29)	< 30 nmol/L	79 (100%)
Alkaline phosphatase, IU/L	40 – 125	985 (265 – 4350)	> 125 U/L	79 (100%)
Calcium, mmol/L	2.1 – 2.6	2.20 (1.28 – 2.10)	< 2.1 mmol/L	29 (36%)
Phosphorus, mmol/L	0.8 – 1.4	0.58 (0.12 – 1.02)	<0.8 mmol/L	34 (43%)
Parathyroid hormone, pmol/L	1.6 – 7.5	9.6 (5.80 – 20.58)	> 7.5 pmol/L	64 (81%)

Younger children had higher proportion of nutritional rickets. Significantly higher proportion of male (85.9%) were rachitic than female (66.7%, p value <0.05). Table 3 and 4 shows relationship of nutritional rickets with age and sex of children respectively.

Table 3 Relationship of age with nutritional rickets among enrolled children (n=79)

Age categories	Nutritional Rickets		*p* value*
	Present n (%)	Absent n (%)	
12 – 23 months	35 (85.4%)	6 (14.6%)	0.47
24 – 35 months	22 (75.9%)	7 (24.1%)	
36 – 47 months	16 (80.0%)	4 (20.0%)	
48 – 59 months	5 (62.5%)	3 (37.5%)	
60 months	1 (50%)	1 (50.0%)	

* *p* value determined by χ^2 test

Table 4 Relationship of sex with nutritional rickets among enrolled children (n=79)

Age categories	Nutritional Rickets		*p* value*
	Present n (%)	Absent n (%)	
Male	55 (85.9%)	9 (14.1%)	0.023
Female	24 (66.7%)	12 (33.3%)	

* *p* value determined by χ^2 test

Of all, 52% child came from urban areas and 48% came from rural areas with diverse level of education of parents. About 32% of parents had no formal education and 30% parents got 1 to 5 years of education. On the other hand, budget deficit (62%) was the most frequent phenomenon in this study populations. For more details, see table 5.

Table 5 Key socio-economic characteristics of children with suspected rickets

Variables	Frequency	%
Residence		
Urban	52	52%
Rural	48	48%
Education of parents (years)		
0	32	32%
1 - 5	30	30%
6 – 10	26	26%
>10	12	12%
Monthly Income		
Deficit	62	62%
Breakeven	30	30%
Surplus	8	8%

Spectrum of initial presentation of nutritional rickets patients varied in our study (table 6). The most common presentation was with rachitic limb deformity wherein 51.9% cases presented with bow leg, 25.3% with knock knee, 27.8% with swelling and widening of wrist and 7.6% with sabre tibia. Delayed growth was identified in 26.6% children followed by delayed dentition (21.5%), rib beading (26.6%) and skull deformity (24.1%).

Table 6 Spectrum of presentation of children with nutritional rickets (n=79)

Presentation		Frequency	Percentage
Lower limb deformity	Bow Leg	41	51.9%
	Knock knee	20	25.3%
	Sabre Tibia	6	7.6%
Upper limb deformity	Double Malleolus	13	16.5%
	Swelling and widening of wrist	22	27.8%
Other deformity	Craniotabes	9	11.4%
	Wide Anterior Fontanelle	10	12.7%
	Rib beading (Rickety Rosary)	21	26.6%
	Pectus Carinatum	20	25.3%
	Delayed Growth	21	26.6%
	Delayed Dentition	17	21.5%

DISCUSSION

Nutritional rickets is acknowledged as a major public health concern globally.[2,8] Bangladesh contributes a major share of the global burden of nutritional rickets. A high prevalence of rickets was reported in Cox's bazaar and in other districts of Bangladesh.[22]

The main reason for nutritional deficiency rickets in Bangladesh was suggested to be calcium deficiency rather than vitamin D deficiency in a previous study.[14] In our study, we included 100 suspected cases of rickets and found 79% cases of nutritional deficiency rickets. In all of them, 25-hydroxy vitamin D level was deficient. Reason for the difference between this study and the aforementioned study could be attributed to sample size and study design.

Deficiency of Vitamin D in nutritional rickets needs to be addressed as several studies reported vitamin D deficiency of 28% to 40% in infants and younger children of Bangladesh depending on the age and weight of the children.[13,23] Also, vitamin D deficiency rickets has re-emerged in many affluent industrialized countries of the world.[2]

About 11% children had rickets due to other causes rather than vitamin D deficiency (non-nutritional rickets) in our study. 25-

hydroxy vitamin D level was within normal range in this group of children and was significantly higher than nutritional deficiency rickets group (p value <0.001). Non-nutritional rickets group possibly consists of hypocalcemic rickets, hypophosphatemic rickets and vitamin D resistance rickets in whom Vitamin D level tends to be high.[24]

Respectively 36%, 43% and 81% nutritional deficiency rickets children had calcium deficiency, phosphate deficiency and parathyroid-hormone excess in the circulation. In contrast, an Australian vitamin D deficiency rickets surveillance study found 12% cases of calcium deficiency, 7% cases of phosphate deficiency and 49% cases of parathyroid hormone excess among 398 children of vitamin D deficiency rickets.[25]This probably was due to concomitant calcium deficiency in our subjects which led to high parathyroid hormone and low phosphate level in the blood.

Consistent with findings of other studies[15,16] nutritional rickets were found more in younger age groups and in male children in this study.

Bow leg (51.9%) and swollen and widened wrist (27.8%) was the leading sign of nutritional rickets in this study. However, Karim *et al.*[14] found knock knee (38%) followed by bow leg (26%) to be the leading presentation of lower limb rickets in their study. On the other hand, a Nigerian study reported swollen wrist to be the leading sign (65%), followed by bow leg (60%).[26]

Our study found a higher frequency of uneducated (32%) and less-educated parents (30% with education between 1 to 5 years) in the suspected rickets children. Although the Cox's bazaar study found a similar picture, lesser number of parent's education year may not be associated with increased incidence of rickets.[22]Because, a Nigerian study found significantly higher education years in fathers of rachitic children.[1]

Majority of the families were running on a monthly deficit budget. Similar findings was reported by Karim and his colleagues.[22] Further carefully designed studies are needed to establish low socio-economic status as a factor of nutritional deficiency rickets.

CONCLUSION

Among the suspected rickets cases there were about 88% patient suffering from nutritional rickets. This findings of this study refuted the common perception of general population and physicians that tropical countries like Bangladesh has lower prevalence of nutritional rickets due to sufficient sunlight exposure. However, this may made scope to study further to evaluate the fact behind this phenomenon and influence of air pollution rather than dietary deficiency alone. A possible preventive approach could be supplementation of active vitamin D_3 along with Vitamin A campaign and raise awareness about fortified food intake and/or introduction of food fortification with vitamin D.

Limitation of the study

- Deficiency or reduced intake of dietary calcium intake was not considered as an etiological factor of nutritional rickets
- Impact of sunlight exposure was not included in this study
- Influence of air pollution was not evaluated
- Evaluation of secondary rickets was beyond the scope of the study

List of abbreviations

ALP- Alkaline phosphatase
DSH-Dhaka Sishu Hospital
NNR-Non-nutritional rickets
NR-Nutritional rickets
PTH- Parathyroid hormone
SD-Standard Deviation
SPSS-Statistical package for social science

Declarations

Ethical consideration

The researcher was duly concerned about the ethical issues related to the study. Formal ethical clearance was taken from the ethical review committee of the Dhaka Shishu Hospital for conducting the study. Formal written consent was taken from the parents of the child. And throughout the study, confidentiality was maintained properly.

Consent of Publication: Not applicable

Availability of data and material: Data and materials supporting our findings in the manuscript will not be shared. It was not in accordance with participants' verbal consent

Competing Interests: The authors declare that there is no conflict of interests regarding the publication of this paper.

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Author Contributions

SPS conceive and developed the concept of the study. Conception and design of this Research were made by AASMNA, MJA and MJH. SPS wrote the first draft of the manuscript and MKH, AT &MJH reviewed the draft. All authors read and revised the article and SPS approved the final manuscript.

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