

Original Research Article

Subclinical rickets among children visiting a tertiary care hospital

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ABSTRACT

Background: Subclinical rickets is the early stage of rickets which can be defined as a state where there are no clinically appreciable changes of rickets but is characterized by biochemical changes which include the following Low or normal calcium, Low phosphorus, raised alkaline phosphatase and Low Vitamin D or raised Parathyroid hormone (PTH) levels. Radiological changes are often subtle to detect in sub clinical rickets. The objective of the present study was to estimate the prevalence of subclinical rickets in the age group 6 weeks to 15 years in tertiary care centre and to study their clinical profile.

Methods: Hospital based Cross sectional study was conducted among 156 children in the age group 6 weeks to 15 years over a period of 1 year at a tertiary care centre in South Bangalore. Evaluation and diagnosis of Subclinical rickets was done using various biochemical parameters such as Calcium, phosphorus and alkaline phosphatase and Wrist X ray.

Results: Overall Prevalence of Subclinical Rickets among the study group was 57 (36.5%). Sub clinical rickets was more common among Females (41.4%). Significant difference was observed in time spent for outdoor activities among children with (7.18±3.2 hrs) and without (9.04±4.4 hrs) subclinical rickets. Vitamin D supplemented group had lower prevalence of Subclinical rickets. 26% of them had Wrist Changes for sub clinical rickets. Significant decrease in Serum calcium and phosphorus was observed between subjects with and without subclinical rickets.

Conclusions: Prevalence of Subclinical Rickets in children aged between 6weeks to 15 years is significantly high. Optimal exposure to sunlight and Vitamin D supplementation can bridge the deficiency gap.

Keywords: Biochemical parameters, Children in tertiary care centre, Subclinical rickets, X ray wrist

INTRODUCTION

Subclinical rickets is the early stage of rickets which can be defined as a state where there are no clinically appreciable changes of rickets but is characterized by biochemical changes which include the following Low or normal calcium, Low phosphorus, raised alkaline phosphatase and Low Vitamin D or raised Parathyroid hormone (PTH) levels.

Radiological changes are often subtle to detect in subclinical rickets.¹⁻⁵ There are several Indian studies on

Rickets and its causes. But, there are very few studies on subclinical rickets from India or other countries. Also, with the increase in tendency of children spending more time indoors watching TV and playing computer games rather than outdoor games, they are minimally exposed to sunlight thereby contributing to Vitamin D deficiency. This coupled with poor intake of foods rich in calcium increases the incidence of rickets.

This study provides an opportunity to detect rickets at its early stages and thus enabling early intervention in

preventing the development of florid rickets and related complications.

This study was done to estimate the proportion of Subclinical Rickets among children visiting a tertiary care hospital in the age group 6 weeks to 15 years, to determine the clinical profile of children with subclinical rickets and to associate the findings of Alkaline Phosphatase, Calcium and Phosphorus in subclinical rickets.

The objective of the present study was to estimate the prevalence of subclinical rickets in the age group 6 weeks to 15 years in tertiary care center and to study their clinical profile.

METHODS

This was a hospital based observational study for a period of one year January 2015 to December 2015 among the children in the age group between 6 weeks to 15yrs, in a tertiary care center of South Bangalore. Both inpatient and outpatient attendants were considered in the study.

Inclusion criteria

- Both inpatient and outpatient attendants were considered in the study

Exclusion criteria

- Children with clinical features of rickets with or without treatment, Renal disease, Liver disease, chronic illness and critically ill were excluded from the study.^{6,7}

Sample size of 100 was estimated by using the prevalence (i.e. 39%) of subclinical rickets from the study by Tanveer Hussain Shah et al was used to obtain the sample size.⁸ Formula used for estimating sample size was $N = (1.96)^2 PQ/d^2$, P = Prevalence of subclinical rickets = 39, Q = 100-P = 61, d = Absolute error = 10%, with 99% confidence level $n = 141$. Expecting 10% Non-compliance sample size $N = 141 + 14.1 \approx 156$ cases were included in to the study.

A total of 156 children who fulfilled the inclusion and exclusion criteria and gave informed consent during the study period were included in the study.

Multi stage sampling method was used to collect data as shown in Figure 1. Prior institutional ethics committee permission was obtained. Detailed Demographic profile, clinical history, physical examination findings, anthropometric findings (Z scores) and laboratory findings was collected by using a semi structured questionnaire. Details of vitamin D supplements were collected. Those who were on either regular dose of 400IU-600IU/day dose or irregular supplements were grouped under children on supplements and the rest as

children not on supplements. 5ml of blood sample was collected in Un-heparinised tube and the results were obtained and interpreted.⁹

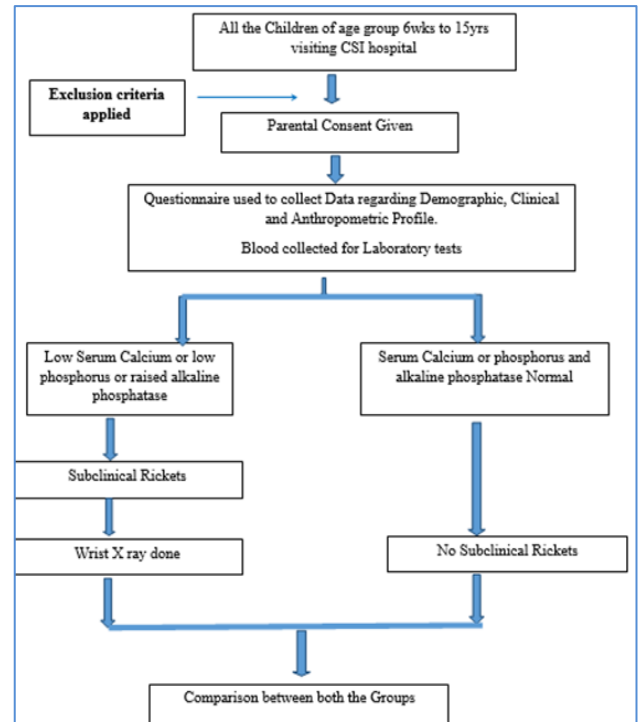


Figure 1: Multistage sampling procedure in the study.

Serum calcium and serum phosphorus was estimated by calorimetric assay and Calcium values 9 to 11mg/dl were considered normal and phosphorus values of 2.5 to 4.3mg/dl were considered normal. Serum alkaline phosphatase was estimated by spectrophotometric method, using 4-nitrophenylphosphate as substrate with alkaline buffer (DEA).

Age and sex specific values which also matched with the standard values of University of Rochester Medical Science were considered normal.¹⁰

Subclinical rickets was considered if any one of the following or in combination was observed. Low calcium (<9 mg/dl) or low phosphorus (<2.5mg/dl) or Raised alkaline phosphatase specific for age and sex. The children who were diagnosed as subclinical rickets by using the above criteria were subjected to X-ray wrist to look for loss of definition of metaphyseal lines, as an additional evidence of subclinical rickets.^{7,11-13} Children with subclinical rickets were treated appropriately, and health education was given to caregivers with respect to nutrition and diet.

Statistical analysis

Data was analyzed using SPSS 22 version software. Chi-square was used as test of significance. Fischer Exact test

was used when chi-square test was not applicable. Quantitative data was represented in the form of Mean and Standard deviation.

Independent 't' test was used to test the significance for quantitative data. p value <0.05 was considered as statistically significant.

RESULTS

In the study out of 156 subjects who were included in the study 57 (36.5%) of them had Subclinical Rickets based in the Laboratory investigations and X ray of Wrist. Mean Age of subjects in the study was 35.91 Months, Median age was 20 months.

Table 1: Comparison of biochemical profile in children with and without subclinical rickets.

		Sub clinical rickets				p value
		Present		Absent		
		Count	%	Count	%	
Calcium	< 9 mg/dl subclinical rickets	49	86.0	00	0.0	<0.001*#
	> 9 mg/dl normal	08	14.0	99	100.0	
	Mean Calcium (mg/dl)	8.57±0.50		9.78±0.45		
Phosphorus	< 2.5 mg/dl subclinical rickets	05	8.8	00	0.0	0.003*#
	> 2.5 mg/dl normal	52	91.2	99	100.0	
	Mean phosphorus (mg/dl)	3.68±0.96		4.49±1.64		
Alkaline phosphatase	Increased	05	8.8	00	0.0	0.003*#
	Normal	52	91.2	99	100.0	
	Mean ALKP (Units/L)	208.04±115.7		183.27±55.34		

Table 2: Association between subclinical rickets and demographic profile of subjects.

		Sub clinical rickets				p value
		Present		Absent		
		Count	%	Count	%	
Age	1 to 11 Months	15	37.5	25	62.5	0.999
	1 to 3 years	25	35.2	46	64.8	
	4 to 6 years	8	38.1	13	61.9	
	7 to 9 years	6	37.5	10	62.5	
	10 to 12 years	3	37.5	5	62.5	
Sex	Female	29	41.4	41	58.6	0.252
	Male	28	32.6	58	67.4	
Month of enrolment	January	1	100.0	0	0.0	0.321
	February	11	36.7	19	63.3	
	March	5	20.8	19	79.2	
	May	3	30.0	7	70.0	
	June	15	57.7	11	42.3	
	July	8	32.0	17	68.0	
	August	1	16.7	5	83.3	
	September	6	35.3	11	64.7	
	October	7	41.2	10	58.8	
Socio economic status (SES)	1	0	0.0	2	100.0	0.353
	2	14	40.0	21	60.0	
	3	29	32.6	60	67.4	
	4	14	46.7	16	53.3	
Religion	Muslim	26	36.6	45	63.4	0.995
	Hindu	17	37.0	29	63.0	
	Christian	14	35.9	25	64.1	
Vitamin D supplementation	Not Received	50	41.3	71	58.7	0.021*
	Received	07	20.0	28	80.0	

Majority of them were males (55%), belonged to Muslim community (45.5%) and 57% belonging to class 3 Socio economic status (Middle class). In the study subclinical rickets diagnosis was made when calcium was <9 mg/dl in 31.4% of subjects, phosphorus <2.5 mg/dl in 3.2%, alkaline phosphatase levels higher than normal for age and gender in 3.2% and by Wrist X ray changes in 6.4% of subjects. It was observed that 86% of subclinical rickets children had low calcium levels, 8.8% had low phosphorus levels and raised alkaline phosphatase levels.

In children with subclinical rickets mean Calcium levels was 8.57±0.50 mg/dl, mean phosphorus levels was 3.68±0.96 mg/dl and Mean alkaline phosphatase levels was 208.04±115.79. Serum calcium levels and serum

phosphorus levels was significantly lower in subclinical rickets children than children without subclinical rickets.

Different age groups in the study had almost same prevalence of subclinical rickets. Females had higher prevalence of Subclinical rickets than males. Age, gender, month of enrolment, religion and socio-economic status did play a significant difference in prevalence of subclinical rickets. Vitamin D supplemented group had significantly lower prevalence of subclinical rickets. Average time spent in outdoor activities was significantly less (7.18±3.2 hrs) in subclinical rickets children than in (9.04±4.4 hrs) children without subclinical rickets. Out of 57 subjects with subclinical rickets, wrist X ray was done in 38 subjects.

Table 3: Association between alkaline phosphatase levels and wrist X ray in subclinical rickets subjects.

		Subclinical rickets present				Total
		Alkaline phosphatase increased		Alkaline phosphatase normal		
		Count	%	Count	%	
Wrist X Ray	Subclinical rickets	5	50.0	5	50.0	10
	Normal	0	0.0	28	100.0	28
Total		5		33		38

$\chi^2 = 16.12, df = 1, p < 0.001^*$ (Fischer's Exact test)

Table 4: Anthropometric findings in the study in relation to subclinical rickets.

		Sub clinical rickets	
		Present	
		Count	%
SD of weight for age	<-3 SD	04	7.0
	-3 to -2 SD	10	17.5
	-2 SD to - 1 SD	18	31.6
	-1 SD to 0 SD	16	28.1
	0 to + 1SD	07	12.3
	1 SD to 2 SD	02	3.5
	2 SD to 3 SD	00	0
	>3 SD	00	0
SD of Height for age	<-3 SD	01	1.8
	-3 to -2 SD	13	22.8
	-2 SD to - 1 SD	14	24.6
	-1 SD to 0 SD	17	29.8
	0 to + 1SD	08	14.0
	1 SD to 2 SD	03	5.3
	2 SD to 3 SD	01	1.8
	>3 SD	00	0
SD of Head Circumference	<-3 SD	00	0
	-3 to -2 SD	04	8.7
	-2 SD to - 1 SD	05	10.9
	-1 SD to 0 SD	18	39.1
	0 to + 1SD	17	37.0
	1 SD to 2 SD	02	4.3
	2 SD to 3 SD	00	0
	>3 SD	00	0

Of them 10 showed wrist X ray changes such as Loss of definition of metaphyseal line (Figure 2). Among those who showed wrist changes 50% had raised alkaline phosphatase and 50% showed normal alkaline phosphatase. Whereas all the 28 subjects who had normal wrist X ray, had normal alkaline phosphatase levels. Alkaline phosphatase was significantly increased in cases of subclinical rickets who also had associated bone changes (Table 3). Table 4 shows the nutritional profile of subjects with Subclinical rickets.

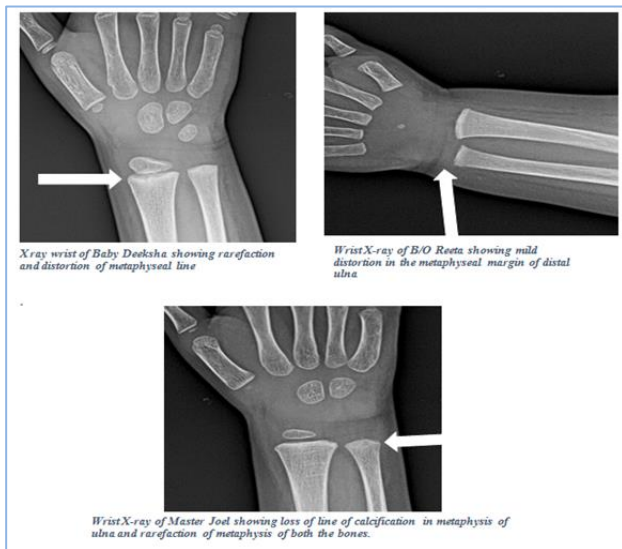


Figure 2: Wrist changes in children with subclinical rickets.

DISCUSSION

Rickets is a well-known disease of growing children prevailing throughout the world. Though there are many studies worldwide regarding rickets, those regarding subclinical rickets is limited. Prevalence of subclinical rickets in the present study was 36.5%, this prevalence is much higher than the 27% that been reported by Shah et al in Pakistan. In another study done by the same authors in Kaghan Valley Pakistan was 39%.^{8,14}

Clinical and demographic profile of children did not play a significant role in prevalence of subclinical rickets. Subclinical rickets was found more in girls than in boys, though this difference was not statistically significant. A similar observation was made by Tanveer Hussain Shah et al who reported subclinical rickets in 15 out of 96 boys (15.6%) and 36 of 93 girls (38.7%) and another study by same authors in Kaghan valley among 11-16 years children 7 out of 34 boys (20%) and 19 out of 33 girls (51%) had biochemical abnormalities of subclinical rickets without clinical signs and symptoms of rickets.^{8,14}

There are no enough studies comparing the prevalence of subclinical rickets and different age groups. The mean age in the study by Seo et al in Korea on sub-clinical rickets was 12.6±5.8 months and age range in the Shah et

al was 11-16 yrs.^{14,15} No significant association between age and subclinical rickets was observed in the present study (Table 2).

Majority of them were from urban areas and were spending less time in outdoor activities. The Studies done in Canada, India and Ethiopia have shown that children from urban areas are more commonly affected and this was attributed to less exposure to sun, because they engage themselves in indoor activities and dress up with minimal skin exposure when outdoors.¹⁶⁻¹⁹ In another study in India identified that indoor confinement during the day, living in urban areas with tall buildings, air pollution, use of sunscreen and covering much or all of the body when outside can be significant risk factors for Vitamin D deficiency and leads to rickets.^{20,21}

In Studies previously conducted in different parts of the world like in Turkey, in Bangladesh and in Kabul made similar observation that rickets was most commonly seen in low socio-economic class.^{22,23} Low socio-economic status leads to low standard of living and limits good care at household level and results in poor growth and development. Low socio-economic status also results in low education which can act as a hurdle for understanding of the disease and early approach to medical facility.

Children who received Vitamin D supplementation had lower prevalence of Subclinical rickets than who did not receive Vitamin D supplementation. Researchers have observed that, vitamin D deficiency is common throughout the world including Southern Europe, the Middle East, China and Japan.⁷ Further, an Indian study found that, about two-thirds of the population had low levels of vitamin D.²⁴ this increase can be attributed chiefly to increased modern lifestyle and less amount of outdoor activities.

In the present study low calcium, low phosphorus and high alkaline phosphatase levels were seen among children with subclinical rickets. Similar findings was reported by Shah et al, who reported Low calcium in 65% and low phosphorus in 27% of their subjects with subclinical rickets. However low calcium level in subclinical rickets was not found by Seo et al.^{14,15} This Korean study also reported a grossly elevated mean alkaline phosphatase of 1995.8±739.5 IU/L, in children with subclinical rickets. Shah et al in his study observed elevated alkaline phosphatase levels in as much as 81% in their cases with subclinical rickets. Were as in the present study 8.8% of them had increased alkaline phosphatase.^{14,15}

Pettifor et al suggested that an X-ray of the wrist is essential to confirm the presence of subclinical rickets and the at-risk infant can be detected by measuring serum Vitamin D (25-OH D) concentrations. Hence in the present study Wrist X ray was performed in 38 children with Subclinical Rickets and it was observed that 26% of

them had Wrist Changes i.e. loss of definition of metaphyseal line.²⁵ Limitations of the study was non-estimation of Vitamin D Levels and Parathormone levels because of its high cost.

In the Absence of Vitamin D and PTH Estimation, Sub clinical Rickets can be considered if following combination of Serum Calcium, Phosphorus and Alkaline Phosphatase though nonspecific for diagnosis of subclinical rickets can be considered, in developing countries where Vitamin D estimation is not financially feasible, these parameters can be used for screening of Subclinical Rickets and in those who are diagnosed as subclinical rickets, Vitamin D can be measured to assist in the further management of subclinical or clinical rickets.

CONCLUSION

Prevalence of Subclinical Rickets in children still remains high and goes unnoticed. Socio demographic does not play a major role in prevalence of Vitamin D, were as Vitamin D Supplementation was associated with low prevalence of Sub clinical rickets. Non-Exposure to outdoor activities had a significant association with increased prevalence of Sub clinical rickets.

Recommendations

The study recommends for routine screening of children for subclinical rickets since it is prevalent in a significant proportion of children, with routine and easily available investigations can be used to diagnose subclinical rickets in resource limited settings like India. Higher outdoor activities in children is recommended by creating awareness among parents and need for regular Vitamin D supplementation and fortification of food products has to be promoted to reduce the burden of this silent disease.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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