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RELATIONSHIP BETWEEN RADIOLOGICAL AND BIOCHEMICAL FEATURES IN CASES OF NUTRITIONAL RICKETS IN INDIAN CHILDREN

Dr. Komalchand gajbhiye[1] & Dr. Binoti sheth[2]

[1]*Lokmanya tilak municipal medical college, Mumbai.*

[2]*Lokmanya tilak municipal medical college, Mumbai.*

Abstract

Introduction: *Rickets is one of the commonest metabolic disorder of growingchildren. In more than 90%,etiology is Nutritional. Disease prevalence is about 50%-90% in developing country like India [(16)]. Commonest complaint that brings the child to orthopedic OPD isthe deformity of lower limbs and wrist swelling. In this study we have analysed the various radiological and biochemical parameters and found out the relationship between these parameters.*

Materials and methods*: Thirty children with age less than ten years, who were showing signs of nutritional rickets were investigated radiologically andbiochemically. The diagnosed cases of nutritional rickets were followed up overa period of six months. The investigations were repeated at 3weeks, 6weeks, 3months and 6 months.*

Results: *Using students't' test and chi square test*,Serum *alkaline phosphatase wasfound to be most important biochemical variables that statistically correlated with active and healing rickets while cupping was found the most reliable sign of active disease.*

Conclusion*: Radiological and Biochemical investigations correlate well with radiological parameters in case of nutritional rickets. Serum alkaline phosphatase is most useful in diagnosis and treatment of the disease.*

Keywords: *Nutritional rickets, rachitic rosary, vitamin D.*

Introduction:

Ricketsis one of the commonest metabolic disorder of the growing children. Disease prevalence is high in developing country like India where more than 90% patients have nutritional rickets.There are very few studies regarding relationship between radiological and biochemical features of nutritional rickets.In this study we have attempted to find relationship between these parameters if any. We studied radiological parameters like width of the metaphysis, cupping, presence of sclerotic bands in the metaphysis and distal diaphysis (also known as growth lines), lossofcoarse trabecular definition and tibio-femoral angle. We also

studied the biochemical features like Serum calcium level, Serum phosphorus level, Serum alkaline phosphatase level and Serum vitamin D 3 levels.

Materials and methods

Thirty children with diagnosed nutritional rickets were studied prospectively over a period of six months at LTMMC Sion.The ageof the patients were ranging from **01- 05 years** with average age being **2.42** years. Among these19 were male and 11were female patients

All suspected children between the ages of 1-5 years, withdocumentedclinico-radiological features suggestive of rickets were included in our study.

Patientsshowing features of other pathological causes of Rickets like renal rickets[1]etc. were excluded from this study.Apart from age, gender, socioeconomic status[2],the duration of complaints and the presence or absence of otherclinical features of nutritional rickets **(FIGURE 1)** like, large broad head, protrusion of the forehead, pigeon chest, rachitic rosary, kyphosis, depressed ribs, widened wrist and presence or absence of limb deformities were noted

Radiological assessment:

Radiological assessment in the form of true size radiograph of both wrist anteroposterior view and both lower limbs full length standing view were taken at the time of presentation, 3 weeks, 6 weeks, 3 months and 6 months.Widthof the metaphysis**(FIGURE3)** was measured at every visit at the widest part of it.Presence or absence of sclerotic bands**(FIGURE2)** in the metaphysis and distal diaphysis was noted at each visit.Cupping and irregularity of the of metaphysis[4]**(FIGURE3**)were looked for at each planned visit.Measurement of tibio-femoral angle[5]**(FIGURE4)** was done from the standing radiograph of the right knee. After marking the centre of the knee joint, the first line was drawn from the centre of the knee along the long axis of the femur and the second line from the center of the knee along the long axis of the tibia passing through the tibial tuberosity the angle between two lines was measured. Analysis of loss of trabecular definition**(FIGURE3**) was carefully done after each radiograph

Biochemical assessment: About 3 ml blood was collected from each child by special physician.Serum 25- OH vitamin D, calcium, phosphorus, alkaline phosphatase analysis[6] were carried out. Serum 25-hydroxy vitamin D (25-OH vit D) was determined according to the method of Scharla using immunodiagnostic Enzyme-Immuno-Assay (EIA) Bensheimand Biomedica, Wien. Kits135.Level ofSerum Alkaline Phosphatase (ALP) was determined according to Moss kits. Serum calcium was measured according to Endres method using Diagnostic Systems International kit1.Serum phosphorus was determined according to Tietz method using Diagnostic Systems International kit138.

After doing the initial biochemical and radiological investigations the children were treated with injection vitamin D 6lac IU orally and oral calcium supplements in the dose of 50-75mg/kg for minimum three months. Usual presentation of rickets is normal to decreased level of serum calcium, decreased level of serum phosphorus, increasedlevel of alkaline phosphatase and decreased vitamin D levels

Statistical methodology:

At the end ofsix months, the radiological and biochemical variables were statistically evaluated for their significance. Students 't'test and chi square test was used for the evaluation.

Results: Association between various radiological and biochemical parameters werestudied and statistically matched, results are as follows.

Table 1: Association between mean metaphysical width and biochemical parameters:

	Mean width of metaphysis (cms)	Serum calcium Level(mg/dl)	Serum phosphorus level(mg/dl)	Alkaline phosphatase IU/dl	Vitamin D ng/ml
At presentation	2.11 ± 0.24	8.66 ± 0.72	3.19 ± 0.68	890.73 ± 168.63	13.00 ± 09.18
3weeks	2.11 ± 0.24	8.94 ± 0.81	*3.97 ± 0.78	*658.37 ± 124.66	*89.53 ± 10.25
6 weeks	2.10 ± 0.23	8.97 ± 0.56	*4.18 ± 0.79	*498.67 ± 110.73	*78.67 ± 08.76
3months	2.01 ± 0.22	*9.07 ± 0.66	*4.51 ± 0.61	*368.43 ± 091.37	*62.20 ± 08.15
6 months	*1.91 ± 0.22	*9.27 ± 0.63	*4.77 ± 0.53	*226.33 ± 065.62	*52.47 ± 07.97

By student t test P <0.05, *Significant

Atthe end of 6 months mean metaphyseal width had significantly decreased (P<0.05) to**1.91 cm**as compared to baseline. Serum calcium level was correlating significantly at 3 and 6 months. Increase in serum phosphorus, alkaline phosphatase and vitamin Dweresignificantly correlating with the width of metaphysis from third week onwards.

Table: 2 Association between cupping and biochemical parameters:

Parameters	Cupping (N=30)		Serum calciumlevel(mg/dl)		Serum phosphorus level(mg/dl)		Alkaline phosphataselevel IU/dl		Vitamin Dng/ml	
Duration	Present	Absent	present(X□ □ SD)	Absent (X□ □ SD)	present(X□ □ SD)	Absent (X□ □ SD)	Present (X□ □ SD)	Absent (X□ □ SD)	Present (X□ □ SD)	Absent (X□ □ SD)
At presentation	29	1	8.69 ± 0.71	07.90 ± 0.00	3.21 ± 0.68	02.50 ± 0.00	890.97 ± 171.61	884.00 ± 0.00	13.17 ± 09.30	08.00 ± 0.00
3weeks	30	0	8.94 ± 0.81	0	*3.97 ± 0.78	-	*658.37 ± 124.66	-	*89.53 ± 10.25	-
6 weeks	29	1	8.93 ± 0.54	10.00 ± 0.00	*4.18 ± 0.80	04.10 ± 0.00	*502.76 ± 110.36	380.00 ± 0.00	*79.24 ± 08.32	62.00 ± 0.00
3months	3	27	*9.09 ± 0.66	08.93 ± 0.81	*4.55 ± 0.53	04.13 ± 1.27	*358.85 ± 084.49	454.67 ± 125.96	*62.70 ± 07.72	57.67 ± 12.42
6 months	1	29	*9.23 ± 0.62	10.20 ± 0.00	*4.79 ± 0.52	04.10 ± 0.00	*226.38 ± 066.78	225.00 ± 0.00	*52.59 ± 08.09	49.00 ± 0.00

By chi square test P <0.05, *Significant

By student t test P <0.05, *Significant

As per this analysis, cupping was present in **96.7%** of cases at the time of initial presentation and remained unchangedtill the end of 6 weeks, after that cupping significantly decreased to 10.0**%** and **3.3%** of cases at 3 and 6 months of treatment respectively. Cupping shared significant correlation with serum calcium level after 3 months whereas serum phosphorus, alkaline phosphatase and vitamin D were correlating significantly from 3 weeks onwards.

Table: 3 Association between sclerotic bands in metaphysis and distal diaphysis and biochemical parameters:

Parameters	Sclerotic bands (N=30)		Serum calciumlevel(mg/dl)		Serum phosphorus level(mg/dl)		Alkaline phosphataselevel IU/dl		Vitamin Dng/ml	
Duration	Present	Absent	present(X□ □ SD)	Absent (X□ □ SD)	present(X□ □ SD)	Absent (X□ □ SD)	Present (X□ □ SD)	Absent (X□ □ SD)	Present (X□ □ SD)	Absent (X□ □ SD)
At presentation	0	30	-	8.66 ± 0.72	-	3.19 ± 0.68	-	890.73 ± 168.63	-	13.00 ± 09.18
3weeks	0	30	-	8.94 ± 0.81	-	*3.97 ± 0.78	-	*658.37 ± 124.66	-	*89.53 ± 10.25
6 weeks	12	*18	9.09 ± 0.53	8.89 ± 0.59	4.16 ± 0.93	*4.21 ± 0.54	472.25 ± 079.69	*516.28 ± 126.44	79.58 ± 07.98	*78.06 ± 09.42
3months	30	0	9.07 ± 0.66	-	4.51 ± 0.61	-	368.43 ± 091.37	-	62.20 ± 08.15	-
6 months	29	*1	9.26 ± 0.64	*9.40 ± 0.00	4.76 ± 0.53	*5.00 ± 0.00	229.62 ± 064.22	*131.00 ± 00.00	52.52 ± 08.11	*51.00 ± 00.00

By chi square test P <0.05, *Significant

By student t test P <0.05, *Significant

As per this study analysis, sclerotic bands were absent in **100.0%** of cases till the end of 3 weeks, but weresignificantly seen in**40.0%** and **96.7%** after 6 weeks and 6 months of treatment respectively. Decrease in the level of alkaline phosphatase and increase in the level of vitamin D shared significant correlation with the sclerotic bands from 3 weeks onwards.

Table: 4 Association between loss of trabecular definition and biochemical parameters:

Parameters	Loss of trabecular definition(N=30)		Serum calcium Level(mg/dl)		Serum phosphorus level (mg/dl)		Alkaline phosphatase IU/dl		Vitamin Dng/ml	
Duration	Present	absent	Present (X±SD)	Absent(X ± SD)	Present (X± SD)	Absent(X ± SD)	Present(X±SD)	Absent(X ±SD)	Present(X± SD)	Absent(X± SD)

At presentation	27	3	8.59 ± 0.70	9.30 ± 0.66	9.30 ± 0.66	2.57 ± 0.60	884.67 ± 168.04	945.33 ± 200.70	12.85 ± 8.82	14.33 ± 14.47
3weeks	27	3	8.93 ± 0.85	9.07 ± 0.21	*4.03 ± 0.77	3.47 ± 0.92	*649.00 ± 114.00	742.67 ± 211.01	*90.48 ± 8.50	81.00 ± 21.52
6 weeks	24	6	8.97 ± 0.61	8.97 ± 0.36	*4.21 ± 0.76	4.03 ± 0.95	*492.21 ± 088.44	524.50 ± 184.74	*77.75 ± 8.64	82.33 ± 09.00
3months	*4	26	8.88 ± 0.73	9.10 ± 0.66	*4.08 ± 0.87	4.57 ± 0.56	*362.75 ± 119.55	369.31 ± 089.24	*51.75 ± 4.35	63.81 ± 07.39
6 months	*3	27	*9.33 ± 0.31	9.26 ± 0.66	*5.10 ± 0.36	4.73 ± 0.53	*220.33 ± 080.16	227.00 ± 065.61	*45.00 ± 5.57	53.30 ± 07.83

By chi square test P <0.05, *Significant

By student t test P <0.05, *Significant

Above observation reveals that, loss of trabecular definition was present in **90.0%** of cases at the time of presentation that remained unchanged till the end of 6 wks, after that it had significantly reduced i.e. only **13.3%** and **10.0%** of cases had loss of trabecular definition after 3 and 6 months of treatment respectively. Loss of trabecular definition correlated with serum calcium at 6 months, rest of the biochemical parameters showed significant improvement with trabeculae from 6 weeks.

Table: 5 Association Between Mean Tibio-Femoral Angle And Biochemical Parameters

	Tibiofemoral angle**(**X ± SD) (N = 30 degree**)**	Serum calcium Level(mg/dl)	Serum phosphorus level(mg/dl)	Alkaline phosphatase IU/dl	Vitamin D ng/ml
At presentation	7.83 ± 1.90	8.66 ± 0.72	3.19 ± 0.68	890.73 ± 168.63	13.00 ± 09.18
3weeks	7.83 ± 1.90	8.94 ± 0.81	3.97 ± 0.78	658.37 ± 124.66	89.53 ± 10.25
6 weeks	7.83 ± 1.90	8.97 ± 0.56	4.18 ± 0.79	498.67 ± 110.73	78.67 ± 08.76
3months	7.70 ± 1.95	9.07 ± 0.66	4.51 ± 0.61	368.43 ± 091.37	62.20 ± 08.15
6 months	7.40 ± 1.98	9.27 ± 0.63	4.77 ± 0.53	226.33 ± 065.62	52.47 ±

	07.97

By student t test P <0.05, *Significant

As per this study data, mean Tibiofemoral angle at baseline was **7.83 degree**which remained same till the end of 6 month as compared to baseline and thus the difference was not significant.Further long term follow up is required to study the change in tibiofemoral angle with time and treatment

Discussion: Nutritional rickets is a form of metabolic bone disease resulting from vitamin D deficiency in children. It causes softening and weakening of bones because of defective or inadequate bone mineralization[7]. Vitamin D is made available to the body by photosynthesis in the skin (endogenous vitamin D from ultra violet ray exposure) and from dietary intake (exogenous vitamin D from dietary or specific supplementation) [8, 9]. Radiological features of rickets includewidening and irregularity of the growth plate ("fraying"), widening of the metaphyseal end of the bone ("splaying"), concavity of the metaphysis ("cupping"). The prominent knobs of bone at the costochondral joints of rickets patients are known as rachitic rosary or beading of the ribs. The knobs create the appearance of large beads under the skin of the rib cage, hence the name by analogy with the beads of a rosary[10].Toddlers and young children are more prone to vitamin-D deficiency because of greater mineral demands of their growing skeletons. A high prevalence has been noted in countries even with adequate sunshine throughout the year. Many of our patients were raised in families of middle or low socioeconomic status. Exclusive breastfeeding [11, 12, 13]without vitamin D supplements for the baby[14], lack of sunlight exposure[15], inappropriate dietary intake and poor housing conditions with lack of ventilation were found to be predisposing factors for the development of rickets.Very few studies have been done to study the relationship between radiological and biochemical parameters in rickets.In a study of sub-clinical rickets in Glasgow infants, Richards et al. (1968) described loss of bony definition and sclerotic bands in the metaphysis which were designated as 'minimal active rickets' and 'minimal healing rickets' respectively and regarded as evidence of sub-clinical vitamin D deficiency.In normally calcified bone, there is well defined trabecular pattern at the metaphysis and distal diaphysis .But in rickets due to formation of large amount of the uncalcified osteoid and due to generalized osteopenia the trabecular pattern is not seen well on the radiograph. Sclerotic bands are also known as growth lines. These growth lines are absent in an active case of rickets but after treatment they gradually appear in the metaphysis and distal diaphysis, which is suggestive of healingof rickets.Itappears after the calcified osteoid is formed in the bone. The authors found a 'weak

relationship' (which was not quantified statistically) between these changes and elevated serum alkaline phosphatase levels. No other biochemical parameters of vitamin D deficiency were considered. In a study conducted by A. Abdul-motaal, an increase in the overall assessed width of the epiphyseal plates bore a highly significant relationship to the dependent variables examined. Serum alkaline phosphatase was most closely related to the severity of radiological rickets and a discriminant function using serum alkaline phosphatase, inorganic phosphorus and the child's age predicted the rachitic category of 100 Asian schoolchildren (56 retrospectively and 44 prospectively) with a high degree of accuracy. Thirty two of the 100 children from both studies had alkaline phosphatase levels over 400IU/1. X-ray evidence of rickets was found in one of the ten children (10%) with levels between400-499IU/1, 9 of the 18 children (50%) with levels between 500-7991U/I and in all 4 children (100%) with levels over 8001U/1.Total serum alkaline phosphatase is presumably the best biochemical indicator of the severity of radiological evidence of rachitic bone disease in a vitamin D-deficient proliferation in the rachitic skeleton. Serum inorganic phosphorus and the calcium-phosphorus product (which was a significant single variable but did not appear in the final discriminant function) reflect the solubility product at the epiphyseal calcification front. Age, which was an independent variable in the discriminant function, was associated with accelerated growth velocity during the pubertal growth spurt in many of the samples of schoolchildren examined. Low serum 25-OHD levels are of little value in predicting the severity of rachitic bone disease. In our study 19 (63.3%) cases were male and 11(36.7%) cases were female. There was no statistical significance between the demographic variables, more number of male cases may be due to our male dominant society where families are more concerned about the health of male child. It was noted that the presentation at the hospital was delayed until there were obvious and sometimes severe deformity in the children. In our study majority of cases had a varus deformity of the lower limb, only 2 children werewith valgusdeformity. In our study radiological features were most closely related to the increased serum alkaline phosphatase, decreased levels of the vitamin D, and decreased levels of phosphorus. But it was less closely related to serum levels of the calcium which was in the normal range in majority of the patients in our study. In our study majority of the cases showedsignificant biochemical recovery from rickets by the end of 3 months .The radiological recovery was also significant after 3 months of treatment suggested by the fact that majority of the patients, cupping was absent by 3 months of the treatment. The sclerotic bands which was consider as a growth line was marked after the 3 months after the treatment. The trabecular definition started to appears after 3 months treatment. The width of

metaphysis was significantly changed by 6 months after starting the treatment. The tibiofemoral angle was unchanged in majority of the patients in speculated duration of the study .Long term follow up is required to see any change in the angle. Serum alkaline phosphatase level shows maximum correlation with the severity of the radiological feature.

Conclusion:

Common clinical presentation of nutritional rickets in Indian children is lower limb deformity. After treatment the deformity takes longer to correct but monitoring radiological and biochemical parameters is essential as there is definite correlation between these two. Serum alkaline phosphatase shows maximum correlation with radiological features from 3 weeks onwards. As seen in most of our patients there is not much change in tibio-femoral angle over six months duration, this parameter may require long term follow up to see any change in the angle as the bone remodeling occurs

Figure: 1 CLINICAL FEATURE OF RICKETS

A: white line of healing **B:** sclerotic band (growth line)

Figure: 2 RADIOLOGICAL SIGNS OF HEALING

Figure: 3 X- RAY SHOWING CUPPING, FRAYING, LOSS OF TRABECULAE AND WIDTH OF METAPHYSIS

Figure: 4 TIBIOFEMORAL ANGLE MEASUREMENT

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