Contributory factors leading to Biochemical change in children suffering from Nutritional rickets.

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ABSTRACT:

Objective: To determine contributory factors leading to biochemical change in selected children suffering from Nutritional Rickets (NR) at Hyderabad.

Methodology This comparative study was conducted from August 2022 to May 2023. Medically diagnosed rachitic children were selected from outpatient department of Liaquat University Hospital Hyderabad. Interviews of patients as well as parents / guardians were conducted through a standard questionnaire. Blood samples were also collected for analysis of Calcium, Vitamin D, Alkaline Phosphatase, Hemoglobin and Phosphorous.

Results: Findings revealed that mostly girls were affected by this disease. Income of parents/ guardians of affected children was Rs. 20,000-Rs. 30,000, consequently balanced diet was not available due to limited income. 53% of children have been dwelling in open houses yet have been suffering from deficiency of vitamin D. Biochemical parameters of NR & control show that mean & standard deviation and p value of Calcium (p-0.004), Vitamin D (p-0.001), Phosphorus (p-0.003) and hemoglobin (p-0.001) have been low and alkaline phosphatase (p-0.002) have been statistical significantly higher than the control group.

Conclusion: Nutritional rickets is a multi-factorial health problem caused by malnutrition of children at early age of life coupled with inadequate mother feeding and other factors i.e. genetics, lack of care etc. Children are our future and we should pay attention to their bone health. National campaign aimed to develop awareness on consequences of risks of low level of Calcium and vitamin D is suggested.

Keywords: Nutritional Rickets, Alkaline Phosphatase, Vitamin D, Early age diet.

Introduction:

"Rickets" also known as Rachitis is a pediatric disorder with characteristics of lack of growth plates and mineralization of bone properly.[1] Microscopic study of rickets shows unmineralization and synthesis of bone matrix. Rickets is mostly diagnosed through clinical parameters and X-ray image.[2] Deficiency of vitamin D, phosphorus or calcium causes rickets. Infant's up to 2 years of age are more vulnerable and adults between 12-15 years are mostly affected by rickets. Rickets have serious consequences for children yet they are often ignored by parents such as growth issues, bone formation, muscle weakness, walking and developmental delay, and dental abnormalities.[3,4] Nutritional rickets (NR) might also be related to deficiency of calcium, vitamin D or phosphorus being essentially required for bone growth.[5] Poor bone density can delay the teething.[6,7] Dietary deficiencies, lack of sun exposure, life style; all are associated with rickets.[8] Some genetic defects that lead to abnormal phosphate homeostasis and cause low phosphate level might also cause rickets.[8] Phosphate provides mineral strength to bones; therefore, it become low if rickets is not treated for long time. Chronic hypophosphatemia causes rickets which develops after 1-2 years of age.[9] The diagnosis of NR depends upon various factors including breastfeeding history, calcium intake, use of supplementary vitamins and minerals, clinical evaluation, biochemical tests and radiography; however; these factors might vary with stage of the disease. Numerous biochemical markers have been utilized for screening and/or diagnosing nutritional rickets including vitamin D, serum and urinary calcium & phosphate levels as well as serum PTH and alkaline phosphatase levels.[10-13] Hemoglobin level should be within normal range during growing age, low level would indicate anemia in children[12] which may cause nutritional deficiency and add to the complications of NR children. One of most common indicators of nutritional rickets is high level of bone alkaline phosphatase in blood. Age and puberty influence reference values on different biochemical parameters.[13]

Objective:

To determine contributory factors leading to biochemical change in children suffering from nutritional rickets at civil hospital Hyderabad through signs, symptoms, history and biochemical analysis.

Methodology:

This is comparative study was conducted from August 2022 to May 2023, after approval from the Ethical Committee of the Institute of Biochemistry; University of Sindh, (Reference no. IOB/293-C/22 dated 13/06/22). The sample size was calculated using OpenEpi calculator. Akram M et al in a study published in year 2022, has reported the prevalence of rickets as 6.90%.[14] With proportion of 6.90%, confidence interval of 95% and 5% margin of error, sample size calculated was 99. For rounding off it was taken as 100. https://www.openepi.com/SampleSize/SSPropor.htm. Control (n=50) were selected from children presenting at outpatient department for some other illness.

For this study; children diagnosed with nutritional rickets aged 1-10 years were selected from Civil Hospital Hyderabad and divided into three age groups i.e., 1-3 years, 4-6 years and 7-10 years. Detailed history asked from clinician, mother/ guardian and subjects according to a questionnaire specially framed for study. This questionnaire com-

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prises of questions on lifestyle, physical activities, parent occupation, nutrition of children, source of drinking water, and clinical examination etcetera. Blood samples were also collected for analysis of calcium, phosphorus, and alkaline phosphatase by photometric method (Modular Analytics; 6000 (Roche) Module C501),[15] Vitamin D by chemiluminescent microparticle immunoassay (CMIA) (ARCHITECT i2000SR immunoassay analyzer),[16] and hemoglobin by photometric method (Sysmex, Hematology, analyzer XP 1000).[17]

Statistical Analysis:

SPSS (version-21) software was used for clinical data analysis.[18] The Mean, Standard deviation, minimum and maximum values of NR patients and control have been determined. Student's T-test used for *p*-value less than 0.05 has been considered statistically significant.

Results:

This study was conducted involving children aged 1 to 10 years, categorized into three distinct age groups: 1-3 years, 4-6 years, and 7-10 years. Among the participants, 44% were boys and 56% were girls, with a notable prevalence of nutritional risk (NR) observed in the 4-6 years age group. The demographic breakdown revealed that 66% of the children identified as Muslims, while 34% were non-Muslims. Parental occupations varied, with 46% employed as laborers, 17% in government positions, 25% in private sector jobs, and 12% as business owners. In terms of monthly income, 35% of families earned between Rs. 10,000 and 20,000, 33% earned between Rs. 20,000 and 30,000, and 32% had incomes exceeding Rs. 30,000. Housing conditions indicated that 53% of NR patients resided in houses, 33% in flats, and 14% in smaller homes. During infancy, 30% of infants were exclusively breastfed, 41% consumed commercial milk, and 29% received a combination of both. Post-infancy, 33% of children drank buffalo milk, 11% cow milk, 22% goat milk, and 34% relied on commercial milk. Regarding breastfeeding duration, 21% of NR patients were breastfed for six months, 32% for one year, 36% for one and a half years, and 11% for two years. Meal consumption patterns showed that 38% of NR children had breakfast, 78% had lunch, and 63% had dinner. Water sources included 38% drinking tap water, 20% groundwater, 17% boiled water, 15% filtered water, and 10% consuming a combination of boiled and filtered water. Rice consumption was reported daily by 21% of NR children, while 33% consumed it twice a week, and others did so occasionally. Vegetable intake was regular for 17% of NR children, while 23% consumed them weekly, and others showed a preference against vegetables. Meat consumption varied, with 30% eating it once a week, 17% twice a week, 23% once a month, 10% regularly, and 20% unable to afford it. Fish was consumed daily by 1% of NR children, twice a week, 15% twice a week, while others very occasionally. It was noted that 57% of children experienced a lack of sun exposure, attributed to changes in lifestyle and irregular sleep patterns. Among NR children, 65% were found to be over one year of age during the teething phase. In terms of walking milestones, 19% of NR children walked between 10 to 15 months, 34% between 16 to 20 months, 40% between 21 to 25 months, and 7% between 26 to 30 months. Additionally, bone malformations were identified in 33% of NR children, predominantly affecting the wrist, knee, and elbow regions.[19]

Age wise distribution (table no 1) indicates that the levels of calcium, vitamin D, phosphorus and hemoglobin are below the normal values, while alkaline phosphatase levels are elevated beyond the normal range for the age group of 1-10 years. This suggests a state of malnutrition among children in this age group. Table No. 2 (Comparison of biochemical parameters of NR & control) indicates that the mean and standard deviation, along with the p-values for calcium (p-0.004), vitamin D (p-0.001), phosphorus (p-0.003), and hemoglobin (p-0.001), are notably lower in the NR group. In contrast, alkaline phosphatase levels (p-0.002) are statistically significantly elevated compared to the control group.

Table no. 1: Age wise overview of biochemical parameters of "NR" group.

Parameters with Normal Ranges	1-3 Years	4 - 6 Years	7 - 10 Years
Calcium (8.6-10.3 mg/dl)	7.3±0.64[a] 6.0-8.4[b]	7.2±0.66[a] 6.0-8.4[b]	7.2±0.75[a] 6.0-8.4[b]
Vitamin D (30-40 ng/ml)	11.8±4.50[a] 3.5-20.3[b]	9.2±4.62[a] 3.2-20.1[b]	8.9±2.57[a] 4.5-13.3[b]
Alkaline Phosphatase 1-3 Years < 409 u/l 4-6 Years < 347 u/l 7-10 Years < 316 u/l	655.9±162.3[a] 415.0-968.0[b]	505.8±169.7[a] 350.0-867.0[b]	503.5±125.9[a] 345.0-694.0[b]
Phosphorous 3.2-5.7 mg/dl	2.2±0.66[a] 1.4-3.0[b]	2.3±0.49[a] 1.4-3.0[b]	2.3±0.48[a] 1.4-3.0[b]
Hemoglobin 6 Months - 1 Year: 9.5-14 g/dL 6-12 years 11.3-14.1 g/ dL	8.58±1.73[a] 6.2-11.1[b]	8.31±1.49[a] 5.5-11.1[b]	9.43±0.72[a] 8.6-10.4[b]

Mean ±SD a and Minimum & Maximum b

Table no. 2: overall comparison of nr effected children (1-10 years) and control group.

Parameters	Control *n*=50 Mean ±SD	NR Children *n*=100 Mean ±SD	P-value <0.05
Calcium (mg/dl)	9.5±0.46	7.26±0.67	0.004
Vitamin D (ng/ml)	34.5±2.80	9.9±4.29	0.001
Alkaline Phosphatase (u/l)	311.2±51.8	550.2±170.4	0.003
Hemoglobin (g/dl)	13.8±0.49	8.69±1.48	0.001
Phosphorous (mg/dl)	4.38±0.55	2.33±0.49	0.002

Discussion:

During current we found that significant number of girls experience nutritional deficiencies relatively at a younger age, potentially attributable to inadequate access to nutrition and health services for females, stemming from gender discrimination within families. Most of the parents of studied children belong to low socio-economic backgrounds, different ethnicities, and face financial constraints along with religious restrictions on food consumption. The varying dietary habits, influenced by income, geographical location, cultural practices, and religious beliefs, may be fundamental factors contributing to the current state of nutritional inadequacy. Furthermore, the quality of life and exposure to sunlight play a crucial role in overall health.[19] The World Health Organization's housing and health guidelines indicate that inadequate housing is linked to a variety of health issues, including tuberculosis, influenza, diarrhoea, and asthma, among others.[20] Insufficient breastfeeding can lead to malnutrition, which may be a fundamental cause of nutritional deficiencies, highlighting the necessity to advocate for and support breastfeeding practices.[10,20] Irregular meal patterns adversely affect the body's nourishment and overall health. Studies have also shown that the quality of drinking water available to nutritionally at-risk children is often poor, with many parents unaware of potential contaminants. While rice serves as a valuable source of calcium and is a crucial dietary element, its improper consumption due to inflation, poverty, and unhealthy habits may lead to calcium deficiencies. Vegetables and meat are essential components of a balanced diet; however, many nutritionally at-risk children exhibit a dislike for vegetables, and meat is often financially inaccessible, limiting its regular consumption. Fish, which is rich in calcium and vitamin D, is rarely included in the diets of these children due to their families' low income. The ideal age for teething in children is between 4 to 6 months; however, nutritionally at-risk children experience delayed teething, which may indicate insufficient bone growth. Additionally, the age at which children begin to walk serves as another indicator of bone development, with healthy children typically walking by 12 months. The delayed walking age observed in nutritionally at-risk children further supports concerns regarding their bone health.[7,21] We found raised alkaline phosphatase, a finding in agreement with published research involving children with nutritional rickets; it has also been shown that the increased serum alkaline phosphatase levels, which correlate significantly with the severity of the condition.[20,21] Consequently, serum alkaline phosphatase serves as a crucial biomarker for the assessment of rickets through blood analysis. Haemoglobin levels are an important health indicator, particularly during childhood development; low haemoglobin levels suggest the presence of anaemia. In this study, the haemoglobin level (8.69±1.48) in the affected children was found to be low, further exacerbating the rickets condition. [22] A balanced diet and the incorporation of supplements may help address various nutrient deficiencies in children, thereby reducing the risk of nutritional rickets.[23-26]

Conclusion:

Nutritional rickets is currently a prevalent disorder in Pakistan, yet most parents are unaware of it. The majority of children affected by NR have been girls from various ethnic groups. Most parents of these affected children belong to low-income communities. Children should engage in outdoor physical activities, including games, to ensure proper sunlight exposure and promote bone health. Children are our future; we must prioritize their bone health. It is recommended that a national campaign be launched to raise awareness about the risks associated with deficiencies in calcium, vitamin D, hemoglobin, and phosphorus in children.

Conflict: No conflict of interest.

Author's Note: "I hereby declare that the given paper is extracted from my MPhil thesis and/or is an extension of my previous research work"

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