Original Article

Frequency and Clinical Profile of Hypophosphatemic Rickets Among Rachitic Children

Taj Muhammad Laghari, Muhammad Ashfaq, Bader-Un-Nisa and Shamsher Ali

ABSTRACT

Objective: To determine frequency and clinical profile of hypophosphatemic rickets among rachitic children at N.I.C.H Karachi, Pakistan.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the National Institute of Child Health Karachi, Pakistan from 21st January 2015 to 20th January 2016.

Materials and Methods: All consecutive children with age 1 to 14 years of either gender having rickets were enrolled. Hypophosphatemia and its clinical profile like short stature, fractures, family history, bony deformity, joint pain, and dental abnormalities were observed.

Results: Out of total 230 rachitic children, frequency of hypophosphatemic rickets were found in 16(7%) rachitic children. The mean age of the patients was 7.56±4.35 years. Majority Gender distribution showed05(31%) were males and 11(69%) were females. Short stature 11(69%), fracture 02(12.5%), joint pain 04(25%), family history of hypophosphatemic rickets was present in 05(31%). Bony deformity and dental abnormalities were found in 07(44%) and 06(37.5%) patients respectively.

Conclusion: In this study, short stature is the most common clinical profile, followed by bony deformities and dental abnormalities. A diagnosis of hypophosphatemic rickets should be considered in all patients presenting with short stature, bony deformities along with low serum phosphate and normal iPTH and 25 – hydroxy vitamin D.

Key Words: Hypophosphatemic rickets, clinical profile, rachitic

Citation of articles: Laghari TM, Ashfaq M, Nisa B, Ali S. Frequency and Clinical Profile of Hypophosphatemic Rickets Among Rachitic Children. Med Forum 2018;29(4):24-27.

INTRODUCTION

Rickets is a worldwide bone disease caused by the problem of mineralization of growing bones in children resulting in bone deformity and growth retardation.[1]Its global prevalence is reported to be approximately 10%.[2] It is stated that calcium deficiency, phosphorous deficiency, or vitamin D deficiency are the most common cause of rickets.[1]In addition, familial history is also reported to be the most important cause of rickets in children.[3]

There are various types of rickets, among these hypophosphatemic rickets have both inherited as well as acquired forms. The "X" linked dominant hypophosphatemic rickets is the most common genetic form caused by mutations in the PHEX gene, which results to increase the level of phosphatonins. This phosphatonins causes renal wasting of phosphate.[4] Some rare hereditary forms of hypophosphatemic rickets are also reported that includes autosomal dominant, autosomal recessive, and hypophosphatemic rickets with hypercalciuria. Moreover, an acquired disorder, oncogenic osteomalacia are usually seen in adults has similar clinical manifestations to the hypophosphatemic rickets.[5]

Patients with hypophosphatemic rickets are resistant to vitamin D therapy and various complications like short stature, bone pain, lower extremity deformity, dental abscesses, enthesopathy, and hearing impairment are reported in these patients.[6]

The rationale of this study is that rickets is common disease in children, an early diagnosis and proper management is required to avoid a lot of morbidity secondary to hypophosphatemic rickets which is an extra economic burden on parents and health facilities of state. Hence thorough investigations and the clinical features of hypophosphatemic rickets, a better understanding and management plan for the disease children could be possible.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted at Pediatric Outpatient department (OPD) and ward, National Institute of Child Health Karachi, Pakistan from 21st January 2015 to 20th January 2016. All consecutive children with age 1 to 14 years of either

National Institute of Child Health Karachi.

Correspondence: Taj Muhammad Laghari, Assistant Professor, National Institute of Child Health Karachi.
Contact No: 0333-3944734
Email: Tajlaghari18@yahoo.com

Received: December, 2017; Accepted: February, 2018

gender having rickets were enrolled. Whereas children already on treatment of rickets and/or receiving antiepileptic (diphenylhydantoin, phenobarbitone) drugs were excluded.

Sample size was calculated using EPI software 6 on the basis of 23.5% prevalence of dental abnormalities in hypophosphatemic rickets in previous study[7], 95% confidence interval, 6% precision. Sample size was found to be 230.

Detailed history from guardians regarding joint pain, fracture, and family history of rickets were taken. Clinical examination was performed by researcher himself for height and weight, joint pain, bony deformities. Fractures and bony deformities were assessed on x-rays and dental examination regarding delayed eruption, dental abscess, and malocclusion were done by dental surgeon having experience of at least five years.

Rickets was defined as softening and weakening of the bones caused by a lack of vitamin D (Serum vitamin D level less than 16pg/ml), calcium (Serum calcium level less than 8.8mg/dl), or phosphate (Serum Phosphate level less than 3.2mg/dl). Hypophosphatemia was defined as serum Phosphate level (PO_4) less than 3.2mg/dl. Short stature was defined as height that is two standard deviations below the mean height for age and sex. Fractures was defined as displacement of bone, were assessed on X-ray. Family history was defined as history of rickets from parents. Bony deformity was defined as presence of genu varum (bowed legs inward in the standing position will be assess clinically and will be confirm on X-ray showing outward bowing of the lower leg of an archers bow), genu valgum (Knee angle in and touch one another when legs are straightened assess clinically and will be confirmed on X-ray showing distal position of the knee joint which bends outward and thus the proximal portion seems to be bent inwards) and coxavara; any of them were labeled as bony deformity.

Joint pain was defined was assessed clinically and presence of Visual analogue score of ≤ 3 was labeled as joint pain. Dental abnormalities were defined as delayed eruption (6 months delay of teeth eruption from its normal period), dental abscess (collection of pus that's from teeth and spread to the surrounding tissues were assessed on periapical X-ray) and malocclusion of teeth; any of them was labeled as dental abnormality.

Statistical package for social sciences (SPSS) version 22 was used for the purpose of statistical analysis. Mean and standard deviation was calculated for age. Frequency and percentage were calculated for gender, hypophosphatemic rickets, short stature, bony deformity, joint pain, fractures, dental abnormalities and family history of rickets. Stratification with respect to age and gender were done. Post stratification chi-square test was applied. P-value ≤ 0.05 was taken as significant.

RESULTS

A total of 230 rachitic children were included. The mean age of the children was 7.56 ±4.35 years.

Majority of children were males (n=124, 53.9%) while 106 (46.08%) children were females.

Table 1: Comparison of Clinical profile of hypophosphatemic rachitic children with age and gender of the patients (n=230).

Variables	Age, years			Gender		
	≤7	>7	p-value	Male	Female	p-value
Short Stature						
Yes	5 (45.5)	6 (54.5)	0.838	4 (36.4)	7 (63.6)	0.513
No	2 (40)	3 (60)		1 (20)	4 (80)	
Fracture						
Yes	0 (0)	2 (100)	0.182	2 (100)	0 (0)	0.024
No	7 (50)	7 (50)		3 (21.4)	11 (78.6)	
Family history of Rickets						
Yes	3 (60)	2 (40)	0.377	1 (20)	4 (80)	0.512
No	4 (36.4)	7 (63.6)		4 (36.4)	7 (63.6)	
Bone Deformity						
Yes	1 (14.3)	6 (85.7)	0.036	2 (28.6)	5 (71.4)	0.838
No	6 (66.7)	3 (33.3)		3 (33.3)	6 (66.7)	
Joint Pain						
Yes	0 (0)	7 (100)	0.002	2 (28.6)	5 (71.4)	0.838
No	7 (77.8)	2 (22.2)		3 (33.3)	6 (66.7)	
Dental abnormalities						
Yes	2 (22.2)	7 (77.8)	0.049	2 (22.2)	7 (77.8)	0.377
No	5 (71.4)	2 (28.6)		3 (42.9)	4 (57.1)	

All data presented as number (%)

Chi-square test applied, p-value <0.05 was taken as significant

Frequency of hypophosphatemic rickets was found in 16 (7%) patients. (Figure 1) A significant difference of hypophosphatemic rickets was observed with respect to age (<0.001) and gender (p-value 0.035). (Figure 2&3)
Clinical profile of hypophosphatemic rachitic children showed that short stature was found 11 (69%) children, fracture in 02 (12.5%), positive family history of rickets in 5 (31%), bony deformity in 07 (44%), joint pain in 6 (37.5%) while dental abnormalities was observed in 7 (44%) children.
Comparison of clinical profile of hypophosphatemic rachitic children with age and gender of the patients showed significant difference in between bony deformity and age (p-value 0.036), joint pain and age (p-value 0.002), dental abnormality and age (p-value 0.049), while gender was only significantly associated with fracture (p-value 0.024). (Table 1).

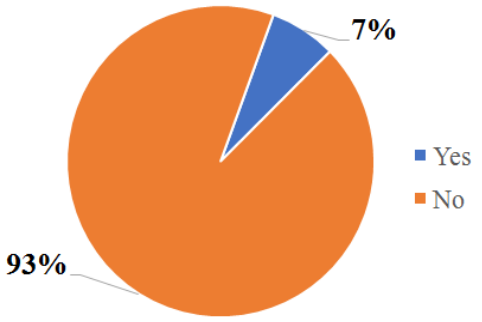

Figure No.1: Frequency of hypophosphatemic rickets

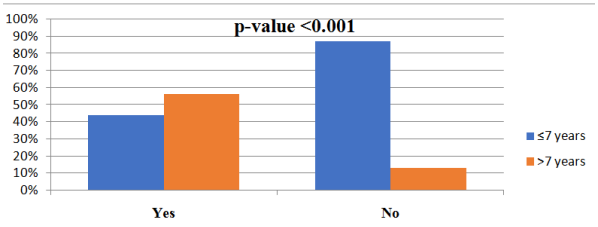

Figure No.2: Comparison of hypophosphatemic rickets with respect to age

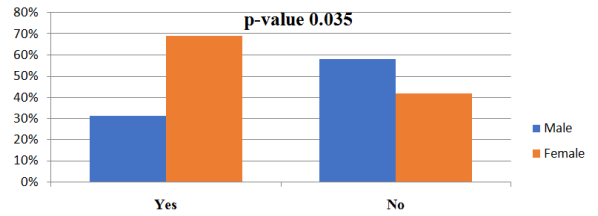

Figure No.3: Comparison of hypophosphatemic rickets with respect to gender

DISCUSSION

Hypophosphatemic rickets is a form of rickets that is characterized by low serum phosphate levels and resistance to treatment with ultraviolet radiation or vitamin D ingestion.[8-10] The findings of our study have showed hypophosphatemic rickets in 7% of the children with rickets. In our study, the presenting age of hypophosphatemic rachitic patients was 7.5 years, which was similar to studies done by Saggese Get al[11] (7 years) and Vaisbich MH et al[12] (6 years).
In our series of patients, hypophosphatemic racket was found higher females (69%),this was similarly reported by Bhadada SK et al (70.5%).[7]This may be due to reason that hypophosphatemic rickets are mostly X linked dominant conditions, which are more common in females.[3]
An outstanding feature of familial hypophosphatemic rickets is short stature, which was reported 69% in our patients and this was found 58.8% by Bhadada SK et al.[7] The short stature associated with this condition is disproportionate, resulting from deformity and growth retardation of the lower extremities. At the time of weight bearing leg deformities (e.g., bowing) are seen. Lower limb involvement is more common.[5]
Fracture 12.5%, joint pain 38% and bony deformities were observed in 44% of our series, while these features were higher in study of Bhadada SK et al which were 29.4%, 52.94% and 58.8% respectively.[7]
In our study family history of rickets was positive in 31% of the children, which was nearly same 35.3% in study conducted by Bhadada SK et al.[7]Dental abnormalities were 44% in our patients and 23.5% were observed in Chandigarh by Bhadada SK et al.[7]
A significant relationship with respect to age and gender in our study revealed that rachitic children were usually diagnosed after 7 years of age,with a greater lag time at diagnosis from the onset of the symptoms. This can be attributed to the lack of awareness to the approach of this entity among the internists and frequent neglect of health-related matters by the ailing individuals. Other than that, most of these patients were treated with cholecalciferol and calcium supplementation for variable period of time without much clinical response. Moreover, it is stated that hereditary hypophosphatemia is rare renal phosphate wasting disorders and its diagnosis is based on clinical, radiological and biochemical features. Furthermore, it may require genetic testing to be confirmed.[13-17]
Fracture was also found significant in our study. However, this feature was only observed in males and not in our female patients. Regarding short stature, bony deformities, dental abnormalities and joint pain, there were no significant difference between male and female children. Bony deformities, dental abnormalities, and joint pain were significantly observed in older age group children, while short stature and fracture have not significantly associated between two age groups.

CONCLUSION

It is to be concluded that short stature is most common clinical profile followed by bony deformity and dental abnormalities in rachitic children. A diagnosis of hypophosphatemic rickets should be considered in all patients presenting with short stature, bony deformities

or musculoskeletal pains along with low serum phosphate level with normal level of iPTH and 25 – hydroxy vitamin D.

Author's Contribution:

Concept & Design of Study:	Taj Muhammad Laghari
Drafting:	Muhammad Ashfaq
Data Analysis:	Bader-U-Nisa, Shamsher Ali
Revisiting Critically:	Muhammad Ashfaq, Taj Muhammad Laghari
Final Approval of version:	Taj Muhammad Laghari

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Jagtap VS, Sarathi V, Lila AR, Bandgar T, Menon P, Shah NS. Hypophosphatemicrickets. Ind J Endocrinol Metab 2012; 16(2):177-82.
2. Beser E, Cakmakci T. Factors affecting the morbidity of vitamin D deficiency rickets and primary protection. East Afr Med J 1994; 71(6):358–62.
3. Rickets GA, Hypervitaminosis D. In: Kleigman RM, Stanton BF, St.Geme III JW, Schor NF, Behrman RE, editors. Nelson Text Book of Pediatrics. 19th ed. Philadelphia: WB Saunders; 2011.p.200-09.
4. Raeder H, Shaw N, Netelenbos C, Bjerknes R. A case of X-linked hypophosphatemic rickets: complications and the therapeutic use of cinacalcet. Eur J Endocrinol. 2008;159Suppl 1:S101-5.
5. Sahay M, Sahay R. Renal rickets-practical approach. Ind J Endocrinol Metab 2013;17(Suppl 1):S35-44.
6. Al Kaissi A, Farr S, Ganger R, Klaushofer K, Grill F. Windswept lower limb deformities in patients with hypophosphataemic rickets. Swiss Med Wkly 2013;143:w13904.
7. Bhadada SK, Bhansali A, Upreti V, Dutta P, Santosh R, Das S, et al. Hypophosphataemic rickets/osteomalacia: a descriptive analysis. Ind J Med Res 2010;131:399-404.
8. Carpenter TO, Shaw NJ, Portale AA, Ward LM, Abrams SA, Pettifor JM. Rickets. Nature Reviews Disease Primers 2017;3:17101.
9. Whiting SJ, Calvo MS, Vatanparast H. Current understanding of vitamin D metabolism, nutritional status, and role in disease prevention. InNutrition in the Prevention and Treatment of Disease. 4th ed. 2017.p.937-967.
10. Fukumoto S. Phosphate metabolism and vitamin D. BoneKEy reports. 2014;3.
11. Saggese G, Baroncelli GI. Hypophosphatemic rickets. Horm Res 2000;53(suppl.3):57-60.
12. Vaisbich MH, Koch VH. Hypophosphatemic rickets: results of a long-term follow-up. Pediatr Nephrol 2006;21:230-4.
13. Manjili FA, Aliabad MH, Kalantar SM, Sahebzamani A, Safa A. Molecular and Biochemical Aspects of Hypophosphatemic Rickets: An Updated Review. 2017.
14. Acar S, BinEssa HA, Demir K, Al-Rijjal RA, Zou M, Çatli G, et al. Clinical and genetic characteristics of 15 families with hereditary hypophosphatemia: Novel Mutations in PHEX and SLC34A3. PloS one 2018;13(3):e0193388.
15. Dhir G, Li D, Hakonarson H, Levine MA. Late-onset hereditary hypophosphatemic rickets with hypercalciuria (HHRH) due to mutation of SLC34A3/NPT2c. Bone 2017 ;97:15-9.
16. Michałus I, Rusińska A. Rare, genetically conditioned forms of rickets differential diagnosis and advances in diagnostics and treatment. Clinical Genetics 2018.
17. Alenazi B, Molla MM, Alshaya A, Saleh M. X-linked hypophosphatemic rickets (PHEX mutation): A case report and literature review. Sudanese J Paediatr 2017;17(1):61.