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Original Article

Evaluation of Osteopenia among the Children with Chronic Diseases at Tertiary Care Hospital of Hyderabad, Pakistan

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Abstract

Background: In recent years, a higher prevalence of bone disease has reported in pediatric population and leads to diagnosis of osteopenia.
Objective: To evaluate the osteopenia among the children with chronic diseases at tertiary care hospital of Hyderabad, Sindh, Pakistan.
Study type, settings & duration: A randomized study was carried out at the department of pedriatrics, Liaquat University of Medical and Health Sciences, Jamshoro and Hyderabad from January to December 2018.
Methodology: The total 214 samples were collected through non-probability convenient sampling technique. Demographic data was noted including age, gender, weight, medical and family history. Data was analyzed by using statistical software SPSS version 22.00
Results: From the collected data of 214 participants, 98 were males and 116 were females. 74 participants were under the age group of 5-8years, 69 in 9-12 years and only 71 were under the age group of 13-17 years. Among all, 65 study subjects were reported with systemic Lupus, 27 with juvenile idiopathic arthritis, 11 with malignant neoplasm, 13 espondioarthritis, neural antibody 17, polymyostis 14, hypermobility among 23 and anti-phospholipid syndrome was found fewer than 14. Total of 98 patients were treated with predisone, 64 with methotrexate and 52 were treated with azathioprine.
Conclusion: It was concluded that osteoporosis among the pediatric patients with chronic diseases was considered as major concern for public health. Early intervention should be provided with calcium administration as well as calcidiol that is economical and has a direct effect on the evolution of osteoporosis from osteopenia.
Key words: Bone mineral density, osteopenia, osteoporosis.

Introduction

A higher prevalence of bone disease (osteopenia and osteoporosis) has been reported in the pediatric population and more so in chronic diseases[1]. Such high predisposition to bone disease in childhood and adolescence occurs due to interference in bone mass formation by various factors.[2] There are currently several techniques for assessing bone mass density but double energy radiological densitometry (DEXA) has been the gold standard in pediatric population.[3] Bone disease in children has been a significant public health concern in a number of countries where prevention and treatment programs are underway.[4] The International Society for Clinical Densitometry (ISCD) proposed that "*low bone mineral density for chronological age*" could be used in people under 20 years of age when the Z-score (adjusted for age, gender and body size) was less than-2 standard deviations (SD).[5] In 2007, a consensus was reached between ISCD expert panelists and renowned practitioners on diagnostic criteria for osteopenia and osteoporosis in children and adolescents aged 5 to 19 years.[6] It was also suggested that the diagnosis of osteoporosis in children should not be based solely on bone mineral density (BMD) values but should take clinical information like bone fractures ,underlying diseases associated with low bone mineral density levels.[7]

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Authors Contribution

KMP conceptualized the project. MF did the data collection. MA did the literature search. VK performed the statistical analysis. Drafting, revision & writing of manuscript were done by MKL & MHA.

Causes of osteopenia or osteoporosis in children are categorized as primary, consisting of a main bone structural alteration due to an intrinsic (usually genetic) bone abnormality; and secondary, due to a systemic or chronic quality-affecting disease of the bone.[6] In case of secondary osteopenia or osteoporosis, various etiological factors can adversely affect the bone growth of children depending upon underlying chronic disease, either alone or in combination with its treatment. Thus, both primary disease and its treatment increases the risk of bone disease and manifestation like osteoporotic fracture.[8] In addition, lack of mobility, inflammatory cytokines induced osteopenia, systemic corticosteroids, disorders of the puberty and malnutrition including obesity may affect the frequency and severity of bone disease. There are various known chronic inflammatory disorders which are associated with low bone mineral density for chronological age or osteoporotic fractures.These are systemic lupus erythematosus (SLE), juvenile idiopathic arthritis (JIA), dermatomyositis, inflammatory bowel disease, neoplasms such as leukemia and various glomerular diseases and endocrine disorders requiring long term immunosuppressive treatment. Increasing cytokine circulating levels such as interleukin (IL) 1, IL-6, IL-7, tumor necrosis factor (TNF) -a, and TNF-B that trigger osteoblast recruitment suppression and stimulate osteoclastogenesis, with the resulting bone turnover imbalance.[9]

Though ,we know the high prevalence of malnutrition and poor lifestyle in Sindh, delayed patient arrival to tertiary hospital with various chronic diseases and their management based on specfic protocols. Therefore, epidemiological data on osteoporosis in Pakistan is scarce since no national registry exist like in developed countries. There is lack of awareness in the treating pediatricians and nonavailability of diagnostic facilities like DEXA at tertiary care centers. Therefore, the study was designed in such a way that can be performed on the pedriatric patients with chronic diseases at Liaquat University Hospital Hyderabad and Jamshoro, Sindh. The main objective of the study was to determine the osteopenia among the children with chronic diseases at tertiary care hospital of Hyderabad, Sindh, Pakistan.

Methodology

The samples were collected from the Department of Pediatrics, Liaquat University of Medical and Health Sciences Jamshoro and Hyderabad, through non-probability convenient sampling technique of 214 patients from January 2018 to December 2018, data collection was collected from the clinical records. Consideration was given to all cases that met the inclusion requirements such as: age 5-18 years both gender, all sex, weight and height determination, chronic illness diagnosis and full clinical record. Records of children who had disease less than 6 months were omitted, because it was the minimum time required to determine any change in the patient's bone mineral density when receiving any medication that affects bone metabolism. Data were obtained from a clinical record of patients. The clinical side factors were: diagnosis and care. The paraclinical and auxiliary research used included: inflammation reactants (PCR and VSG), serum electrolytes (calcium, phosphorus, and magnesium), and DEXA bone densitometry. Even account was taken of socio-demographic variables such as birth, age and sex; and anthropometric variables such as height and weight.

Statistical research was carried out using version 22 of the Windows Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, United States). For continuous variables, means and standard deviations were calculated, and for anomalous distributions the median, range and percentiles were determined. The Student's T test was used to equate a quantitative variable to a two group qualitative one. The Chi test with the Yates correction and the Fisher exact test was used for comparison of two qualitative variables. At an interval of 95%, *p*-value less than 0.05 was considered significant. Prior to performing the research, the permission was taken from the subjects' guardianship. This research was carried out according to the principles of the Declaration of Helsinki.

The Ethical approval was obtained from Research Ethics Committee of Liaquat University of Medical & Health Sciences, Jamshoro.

Results

Table-1 shows gender wise ditribution where majority (54.20%) were females. Almost 35% of patients were between 5-8 years of age while 33% were between 13-17 years as shown in Table-2. Most of the patients reported systemic lupus followed by other diseases as explained in Table-3. A highly significant association ($p \leq 0.001$) was found between raised ESR and raised CRP of the subjects (Table-4).

Treatment modalities in children with chronic disease and the effect on bone health is also presented in the results. It shows that 46% of

the patients were treated with prednisone, 30% with methotrexate and 24% received azathioprine.

Table 1: Gender wise ditribution of study subjects.

Gender	*N*	*%*
Male	98	45.79
Female	116	54.20

Table 2: Age wise distribution of study subjects.

Age Group	*N*	*%*
5-8 Year	74	34.57
9-12 Year	69	32.24
13-17 Year	71	33.17

Table 3: Frequency of chronic diseases among study subjects.

Chronic Disease	*N*	*%*
Systemic lupus	65	30.37
Juvenile Idiopathic arthritis	11	5.14
Malignant neoplasms	13	6.07
Espondio arthritis	17	7.94
Neural antibody	09	4.20
Henoch schonlein purpura	14	6.54
Polymyostis	23	10.74
Hypermobility	21	9.81
Antiphospho lipid syndrome	14	6.54

Table 4: Value of Inflammation reactant among the patient with osteopenia.

Inflammation Reactant	N	%	*p*-value
Raised CRP	92	42.99	<0.001
Raised ESR	122	57.00	

Table 5: Effect of treatment of BMD/DEXA on bone health.

	All patients	*Group 1*	*Group 2*	*p-value*
BMD	0.93±0.16	0.96±0.14	0.82±0.15	0.008*

Table 6: Baseline, 6th and 12th month bone mineral density.

	Baseline	*6th month*	*12th month*	*p-value*
BMD	0.93±0.16	0.93±0.14	0.92±0.13	0.106

The average duration of these medications was 18 months with expected duration of 14 months. A highly significant association ($p \leq 0.001$) was also found between treatment option used by the subjects. Effect of treatment of BMD/DEXA on bone health also presented significant association ($p = 0.008$) while a non significant association can be seen between baseline, 6th and 12th month bone mineral density (Table-5 & 6).

Discussion

The World Health Organization defines osteoporosis as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture risk, but only BMD can currently be objectively measured in clinical practice.[10]

In the current research, patients diagnosed with SLE were found to be the most predisposed to osteopenia, and patients diagnosed with any type of malignant neoplasm and undergoing chemotherapy were more likely to experience osteoporosis and spontaneous fractures. We agree with other researchers that, because of both the disease and treatment, paediatric SLE patients have a higher risk of developing osteopenia. This is clarified by the fact that corticotherapy is still the basis of treatment for this disease and is often used for extended periods at high doses. It is also necessary to remember that the patient needs to prevent sun exposure in this pathology, which also leads to a reduction in bone mineralization.[11,12] In various investigations from the 1990s, beginning with the small cohorts of Dhillon et al in 1990 and Kalla et al in 1993,[13,14] continuing with bigger groups till the present, varying percentages of osteoporosis and osteopenia were recorded for individuals with systemic lupus erythematosus. Osteoporosis prevalence ranges from 1.4-68%, pointing to a widespread loss of bone mass in SLE patients. The variations across studies might be attributed to sex, age, menopausal status, ethnicity, illness duration and activity, and ethnic group.[15] One cohort,[16] which consisted mostly of premenopausal women, had a prevalence of osteoporosis of 36% and osteopenia of 40% of cases, findings that are consistent with those reported by other previous investigations. SLE was shown to be a condition mostly affecting females in their third decade in Pakistan, which is consistent with global statistics. The average age at presentation was 31 years, and the average length of follow-up was 34 months.[17]

It should be noted that in virtually all of the chronic disease treatment lines described in this study, corticosteroids are present. This causes numerous effects on calcium and bone metabolism. They operate on osteoclasts and decrease bone formation; they also inhibit osteoprotegerin, which, through inducing osteoclastogenesis, results in increased bone resorption; decrease intestinal

calcium absorption and increase tubular renal excretion.[18] Corticosteroids may also cause growth retardation, leading to puberty retardation. These medications primarily impact the trabecular bone, causing a reduction in bone mineral density, resulting in accidental fractures or compression fractures.[19] Glucocorticoids, which are taken for lengthy periods of time to enhance survival and quality of life, can induce osteoporosis, particularly in areas rich in trabecular bone, such as the lumbar spine, resulting in a high fracture risk.[20] The effect of corticoid medication on bone loss in SLE patients was examined in several research, including large and small cohorts. Some scientific studies found no correlation, while others discovered a significant relationship.[21,22]

While this study showed no statistical significance in relation to corticosteroids as compared to other medications in relation to the predisposition to osteopenia, it is difficult to know the real effect on the bone structure of any of the medicines provided as monotherapy, primarily because the majority of patients were treated with different types of medicines. It must be treated based on the cause concerned with regard to the diagnosis of osteopenia and osteoporosis due to other conditions and/or medications.

Studies related to paediatric pharmacotherapy for osteoporosis are relatively recent. Calcium and vitamin D supplementation may be adequate in mild cases, but more potent therapies are required for more serious cases. The use of growth hormone, calcitonin, and bisphosphonates are among the newest methods of pharmacological intervention for juvenile osteoporosis.[23]

Biochemical indicators of bone metabolism have been used as evaluation parameters in several investigations,[24–26] in others, bone densitometry or quantitative computed tomography have been used. The causes of corticosteroid-induced osteoporosis are not well known.[27] Individual or genetic vulnerability to bone loss, as well as baseline bone density prior to steroid therapy, may all have an impact on bone density.[28] Luengo *et al*.[29] used dual energy x-ray absorptiometry to evaluate BMD in asthmatic patients treated with 300-1000g day-1 inhaled beclomethasone or budesonide to BMD in age-matched healthy participants at 2 years. There was no statistically significant difference in BMD loss between the patients and the healthy controls. They discovered no link between inhaled steroid dosages or treatment duration and BMD levels. In our research, there was no significant change in BMD of asthmatic patients taking medium or high dosage ICS at the conclusion of one year of treatment.

Some of our patients were eligible for calcium and vitamin D replacement therapy, but there were limited cases where bisphosphonates can be used. Our study accounts for 14% of the overall number of patients in both pediatric facilities. This seems to us to be a decreased figure associated with the inability to include cases of patients with insufficient treatment, patients with long-term follow-up appointments, incomplete or lost records, and perhaps because the patient identification numbers were not present.

The limitation of our study was that it was a cross-sectional design, so the prevalence of osteopenia and osteoporosis in paediatric patients with chronic inflammatory diseases could be underestimated. In addition, the measurement of serum levels of vitamin D, FGF23 and other factors are useful in the study of bone mineral disorders.

In terms of general health and child development, we may infer that the problem of osteopenia and osteoporosis in the child population is significant. Early management should include calcium delivery as well as calcidiol, which is inexpensive and has a direct influence on the progression of osteoporosis from osteopenia. As a result, boosting awareness about bone health in youngsters, as well as creating effective preventative and treatment approaches, is critical. As a result, it was established that osteopenia was prominent among children with chronic diseases at a tertiary care hospital in Hyderabad, Sindh, Pakistan.

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