Review Article

Epidemiological Trends in Pediatric Osteoporosis

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ABSTRACT

Recent advances include understanding bone fragility's genetic and molecular basis and discovering acquired causes of pediatric osteoporosis. Genetic pediatric bone defects are common and morbid, causing osteoporosis. Due to the rising prevalence of chronic diseases like Duchenne muscular dystrophy and immobility, as well as the use of drugs like steroids that can damage bones, secondary osteoporosis in children is rising. Early detection of osteoporosis in children is essential for diagnosis and treatment. Dual-energy X-ray absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT) scan for bone densitometry and vertebral fractures in pediatric osteoporosis patients. Pediatric osteoporosis requires a comprehensive team of bone disease specialists. A specialist should prevent and cure fragility fractures and improve patients' quality of life. Bisphosphonates, the most often recommended drugs for children, enhance BMD and restructure spinal fractures when given promptly. Raising awareness of osteoporosis risk factors, screening youngsters, and referring them to a specialist can detect silent fractures early and avoid bone degeneration. This article reviews childhood osteoporosis and its epidemiology. The global sickness classification and study program are briefly explained.

Keyword: Osteoporosis, pediatrics, Vertebral Fractures, Primary Osteoporosis, Secondary Osteoporosis, DXA, Bisphosphonates.

Introduction

Osteoporosis is a serious health issue that is becoming more prevalent across the world. Due to the fractures caused by the disease, this morbidity problem has significant social, medical, and financial ramifications. Despite being a significant contributor to morbidity, mortality, and disability, osteoporotic fractures are avoidable. Osteoporosis is a recognized clinical issue for individuals across the world. On the other hand, osteoporosis (OP) in youngsters is becoming more well recognized as a serious issue and as a precursor to OP in adults. OP is now understood to affect children as well, despite earlier beliefs that it mostly affected older patients and adults with chronic illnesses [1].

Pediatric osteoporosis is getting greater attention. Hereditary and acquired pediatric bone abnormalities diminish bone density and cause fractures [2]. Lifelong bone formation and degeneration occur. Bone mass accumulates fastest throughout puberty, and 90% of peak bone mass (PBM) is reached by 20 [3]. A 10% rise in adolescent PBM predicts adolescent osteoporosis and prevents postmenopausal osteoporosis by 13 years. Osteoporosis prevention is best throughout childhood and adolescence [4]. Poor bone mass and strength increase fracture risk. Young and old have the highest fracture rates. After 50, women fracture twice as often as men. Children suffer most traumatic long bone fractures. In this population, bone mass and degeneration are substantial risk

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Factors for fracture [5]. Before they reach adulthood, more than 50% of kids will break a bone, and 20% will break several. Paediatric osteoporosis is described as "...an intrinsic skeletal issue resulting in bone fragility" by the Paediatric Positions Task Forces of the International Society of Clinical Densitometry (ISCD) [6]. The 2013 ISCD working group's paediatric positions address paediatric osteoporosis. These methods characterise an infantile fracture as having infantile osteoporosis [7]. However, ISCD standards to diagnose osteoporosis in children have been questioned recently [8]. Recent research proposes considering underlying illness and fracture risk, glucocorticoid use, genetic condition symptoms, fracture site, and BMD trajectory. If children gain bone mass and osteoblast deposition surpasses osteoclast resorption. Due to genetics or secondary causes, osteoporosis disrupts this balance, causing low bone mass and mechanical stress [9]. The term "primary osteoporosis" refers to a group of inherited diseases that make bones more brittle. The most typical cause of primary osteoporosis in children is osteogenesis imperfecta (OI), a group of illnesses characterised by flaws in type I collagen synthesis or processing. Osteogenesis imperfecta is the most prevalent kind of primary osteoporosis in paediatric patients, with a prevalence of 1:15-20,000 births [10]. The main causes of secondary osteoporosis are chronic illnesses or the treatment for them. The most prevalent kind of secondary osteoporosis, which is prevalent in children with cerebral palsy (CP), is disuse osteoporosis. Fractures occur in 6% to 50% of CP patients, and the risk rises with severity [11]. The 2013 ISCD definition protects against over diagnosing and treating youngsters without skeletal fragility. Most pediatric osteoporosis treatments should be used cautiously [8]. Investigations that are practical include bone biochemistry, spine radiography, peripheral QCT, scans for assessing vertebral fractures and bone densitometry. A multidisciplinary team of medical experts with experience treating pediatric bone problems is also required for the treatment of pediatric osteoporosis. In addition to preventing and treating fragility fractures, a specialized service should concentrate on enhancing patients' quality of life. The drugs that are most frequently prescribed for kids are bisphosphonates, which, when administered right away, can increase BMD and realign vertebral fractures [12].

Normal bone physiology

Bone growth and remodeling are challenging because bone is dynamic. Bone is principally composed of minerals, organic matrix, primarily hydroxyapatite, 20–40% collagen, water (5–10%), and lipids (3%). The mineral component offers bone strength and stiffness, whereas the organic matrix gives it elasticity and toughness [13]. Trabecular bone, which resembles a honeycomb, makes up the inner skeleton, whereas cortical bone makes up 80%. Trabecular bone makes up 20% of bone mass but has a much bigger surface area and a faster turnover than cortical bone. Thus, real osteoporotic fractures are more common in sites of bone loss with metabolically active trabecular bone, such as the vertebrae and hip [14]. Numerous cell types, such as osteoclasts, osteoblasts, osteocytes, osteomorphs, and bone lining cells, can be found in bone tissue [15]. Bone modelling encompasses bone production, metaphyseal in wasting, and pelvic bone drift modelling. Osteoblasts or osteocytes secrete osteoid, usually type I collagen, which is mineralized to form mature bone matrix. Bone remodeling replaces old bone in 3 steps. Osteoclasts resorb bone to release calcium and phosphate. Osteoblasts form on the bone in the second phase. Osteoblasts synthesise osteoid, which is mineralized to generate mature bone matrix in the third and final phase [15]. RANK-RANKL, WNT-signaling, and TGF-β signaling pathways control bone production, resorption, and remodeling [15]. Childhood Osteoporosis: The typical early-onset primary osteoporosis is called osteogenesis imperfecta (OI). Primary and secondary causes are frequently distinguished in paediatric osteoporosis [16].

Primary Osteoporosis

Hereditary bone fragility and abnormal bone tissue composition cause primary osteoporosis. Genes affect collagen type I production, bone mineralization, osteoblasts, and osteocyte dysfunction. Early detection is essential for treatment and specialized care [15]. Osteogenesis imperfecta (OI) causes most primary osteoporosis. Clinical traits include recurrent fractures, skeletal defects, short stature, hearing loss, blue sclera, dentinogenesis imperfecta, and ligamentous laxity. Kinds 1–5 of OI are the most common types, and 85–90% of cases are caused by mutations in COL1A1, COL1A2, or IFITM5, which are passed down by autosomal dominant inheritance [15].

Secondary Osteoporosis

Drug use or underlying conditions may cause secondary osteoporosis. The most frequent causes include immobility, thalassemia, hypogonadism, Duchenne muscular dystrophy (DMD), inflammatory disorders treated with steroids, and other myopathies. The most common culprits are proton pump inhibitors (PPI), corticosteroids, and anticonvulsants since they reduce bone mineral density and increase the risk of fractures. Thanks to medical progress, patients with chronic disorders now have longer lifespans [12].

Osteoporosis pathogenesis depends on the cause. Acute lymphoblastic leukemia cells produce cytokines, which increase osteoclast activity, causing 16% of children to develop vertebral fractures (VFs)

when diagnosed [17]. Future fractures are substantially predicted by VFs in the first two years following diagnosis. In order to identify asymptomatic VFs, forecast future fracture risk, prevent vertebral abnormalities, and reduce long-term morbidity, lateral spine imaging is advised for up to 45% of children with VFs [18]. A paediatric bone specialist must monitor Duchenne muscular dystrophy patients due to immobility, extended steroid use, and hypogonadism [19]. Glucocorticosteroids (GCs) cause bone loss by increasing bone resorption and decreasing bone formation [20].

Clinical Signs of Osteoporosis and Laboratory Work Up: A thorough medical history is required from any youngster suspected of having osteoporosis. Analyse the fracture history, paying attention to the number, position, cause, and radiography. Disc fractures can result in back pain. Anthropometry should be part of a physical examination [21].

Children who have been referred for bone health screenings should have their serum levels of calcium, phosphate, magnesium, creatinine, ALP, GGT, 25-hydroxyvitamin D, and PTH, as well as their urine calcium, phosphate, and creatinine levels, all of which should be assessed. Targeted, whole exome, and RNA sequencing should examine osteoporosis without a secondary aetiology. Bone pain or fractures may be symptoms of an illness. As a result, it is recommended to screen for a number of disorders, including celiac disease, ESR, CBC with leucocyte differentiation, serum TSH, and free T4. LH, FSH, testosterone, and estradiol tests should be performed as well as those for Cushing's disease and 24-hour urine cortisol [16].

Methods

Bone Health Diagnostic Methods

Dual Energy X-Ray Absorptiometry (DXA): (Axial and appendicular skeletal health): The most popular and accessible approach for determining a child's bone mass and density is DXA [22]. Currently, lateral distal femur BMD Z-scores can help youngsters with neuromuscular diseases who prefer to lie on their side. The LS and the entire body less the head continue to be the primary measuring points [23]. Raw BMD data are transformed into Z-scores, which must be evaluated in respect to body type, ethnicity, pubertal staging, and skeletal maturity (as defined by bone age) [24]. Z-scores are age- and sex-specific Standard deviation ratings. To avoid underestimating BMD parameters in children with familial short stature and children with chronic illnesses who may be short temporarily or permanently due to the disease/treatment's effects on linear growth and puberty, bone mineral apparent density (BMAD), volumetric BMD, in g/cm3, or height-corrected BMD Z-scores should be used [25, 26].

Radiography: Scoliosis and VFs are both found via radiography. Contrary to adult recommendations, which state that back discomfort alone does not provide a reason to undertake imaging, lateral spine imaging and a concealed VF investigation should be carried out in all children with suspected osteoporosis [27]. VFs are often evaluated using the semi-quantitative Genant technique. This approach is based on visual assessment of morphological change and calculation of spinal height reduction [28]. Vertebral height loss greater than 20% is indicative of VF, with height loss of 20–25% considered mild, 24%–60% considered intermediate, and > 40% considered severe. According to recent research, the most recent DXA scanners can also spot mild to severe VFs cases in children through the measurement of vertebral fractures while emitting lower radiation doses than lateral spine scans [29].

Peripheral Quantitative Computed Tomography (pQCT): (Appendicular skeletal health) pQCT provides (at the radius and tibia) "true" (volumetric) cortical and trabecular BMD and musculoskeletal geometry that DXA cannot. The predominant structural defect in cerebral palsy children is reduced bone and cortical cross-sectional area, not decreased cortical BMD. Growth hormone shortage and therapy affect cortical thickness, not density, according to pQCT studies [30]. pQCT is useful when spine deformity, hip and knee contractures, or metallic devices prevent DXA. High-resolution pQCT can evaluate microarchitecture and trabecular geometry. Most research centres utilise pQCT and high-resolution pQCT [31].

Bone Turnover Markers (BTM): BTM are not a part of the usual osteoporosis workup for children. BTM are challenging to analyze since they have a strong correlation with growth velocity. In rare circumstances, abnormal BTM (with suitable reference data) may offer diagnostic hints [32]. Children with OI may have high levels of bone resorption indicators, which are correlated with a high rate of trabecular bone development on trans-iliac biopsies. On prolonged GC treatment and in juvenile osteoporosis caused by LRP5 mutations, there have been documented reductions in bone resorption indicators and poor trabecular bone production [33].

Fracture Features and Clinical Circumstances That Support The Necessity For A Bone Health Examination And Offer Evidence For An Osteoporosis Diagnosis

Non-Vertebral Fractures: Between birth and age 16, the fracture risk for boys is 42%-64%, compared to 27%-40% for girls. According to every epidemiological study, the forearm accounts for half of all fractures. Children's upper extremities account for 65% of long bone fractures, whereas their lower

extremities account for 7% to 28% of cases [6]. The continual lag between mechanical stressors that generate bone tissue strain and compensatory changes in bone structure that enhance bone strength in response to tissue strain may be the source of the increased fracture rate in children [6]. Due to the high occurrence of long bone fractures in young people, the ISCD 2013 Position Statement defined a major fracture history as two or more by age 10 or three by age 19. For a youngster that exhibits neither physical symptoms of bone fragility nor risk factors, these rates are reasonable. However, while determining whether to begin a full bone health evaluation or diagnose a kid with osteoporosis, it is important to consider the location, radiographic characteristics, and clinical context of the child's long bone fracture. It's important to find a lengthy bone fracture. In a child with OI or risk factors like Duchenne muscular dystrophy (DMD), even a single low-trauma long bone fracture can result in osteoporosis. The main way lower extremity fractures interfere with daily living is with mobility. Even while a single tibia or humerus fracture in an individual at risk for osteoporosis may indicate an osteoporotic event and necessitate further evaluation, low-trauma femur fractures are particularly challenging [8]. Only persistent forearm fractures in young children necessitate a bone health assessment, barring risk factors (like DMD) or OI stigmata (like blue sclera). No matter where the long bones are located, comminuted fractures and those with aberrant displacement are serious, particularly if they occur without trauma. Importantly, regardless of where a child's fracture is located, the risk of intended trauma should be thought. This is particularly true if the fracture occurs before the age of two, there are delays in seeking medical attention, the clinical examination reveals unknown injury to or other injury-related symptoms, such as retinal haemorrhages, there are multiple fractures in various stages of healing, or the identified system of trauma is irrelevant to the type of damage [8].

Vertebral Fractures: The 2013 ISCD Position Statement supports the idea that osteoporosis is compatible with 1 VF, which is defined as a drop of > 20% in vertebral height ratio using the Genant semi-quantitative technique. This was backed by the 2019 ISCD Position Statement. Paediatric VF are uncommon in children without trauma, however they can happen to 75% of kids with OI from COL1A1 haplo-insufficiency mutations, 13% of kids with leukaemia, > 50% of boys with DMD treated with GC, and 16% of kids who are fracture-prone but otherwise healthy. In a study of children with leukaemia, genant-defined VF at diagnosis was associated with recent vertebral and long bone fractures, suggesting its potential use in VF detection in young patients. Due to the fact that VF can serve as an early indicator of major systemic diseases such leukaemia and inflammatory disorders, the 2013 ISCD advice that even one VF can suggest childhood osteoporosis is crucial [8].

Prevention Of Osteoporosis In Children: Despite the fact that the primary drivers of PBM acquisition are inherited and/or influenced by other illnesses and their associated therapies, we may influence the elements that can be positively influenced in developing youngsters. Inadequate calcium and vitamin D consumption, increasing physical activity, managing underweight or obesity, addressing endocrine disorders, and avoiding osteo-toxic drugs such glucocorticoids when feasible can all help to prevent suboptimal PBM acquisition [34]. Calcium, the bone matrix's building block, is essential for mineralization. Calcium deficit releases parathyroid hormone, which mobilises bone calcium and hinders bone development. Depending on their diet, children with osteoporosis may need more than 1,000 mg of calcium daily. Dietary calcium is best. Calcium supplementation for chronically unwell youngsters is also unproven. Intestinal calcium and phosphorus absorption is decreased by vitamin D deficiency [35]. 600 IU of vitamin D2 or D3 is advised for children aged one to 18 at risk of vitamin D deficiency due to inadequate sun exposure, mal-absorption disorders, or anticonvulsant medication.40 For at least six weeks, children aged one to 18 with vitamin D deficiency (serum 25(OH)D levels below 20 ng/ml (50 nmol/l) should take 2,000 IU of vitamin D daily. After that, 600–1,000 IU per day is recommended to maintain 25(OH)D levels between 30 and 50 ng/ml. Some persons need two to three time's higher dosages to achieve appropriate serum levels [35]. If osteoporosis and fracture prevention methods are insufficient, the question of whether to administer bone-active medications may come up. Although the effectiveness and safety of these treatments have been fairly well studied in the adult population, there is less information available on their use in treating children. Recombinant parathyroid hormone, the solitary anabolic bone treatment present, is not permitted for use in children since it has been linked to osteosarcoma in developing rodents. The sole other option is a class of drugs called bisphosphonates that are active against catabolism of bone [34]. While bisphosphonate therapy is increasingly common for children with OI, less is known about its effects on kids who have secondary osteoporosis. Data on efficacy, safety, agent selection, treatment length, and long-term results are lacking. As a result, only sizable pediatric facilities should administer bone-active drug treatment to children, and clinical trials are preferred [34].

Management Of Osteoporosis

Bisphosphonates (BPs): BPs are artificial pyrophosphate analogues that prevent bone resorption. They focus and raise BMD specifically in skeleton regions with significant rates of skeleton remodeling. They are hydrophilic medicines that are eliminated in urine and have minimal intestinal absorption (less than 1%). As a result, dosages need to be changed in accordance with glomerular filtrate. They slowly destroy bone tissue and can stay in the body for years after treatment. Understanding of medium- and long-term drug safety is expanding. Therefore, if the osteoporotic criteria are satisfied, some writers advise using them, particularly in those with long bones and VF who have a low probability of a natural recovery [36]. Up until now, BPs have only been recommended as a supplement to prevention. They avoid fragility fractures following the fracture. We are looking into their long-term safety because we are aware that they increase BMD. Poor peak bone mass towards the end of growth, however, could result in osteoporosis later in life. Patients without osteoporosis who have poor BMD throughout early puberty, low Z-scores, and decreasing trajectories are advised to take BPs [36]. For paediatric osteoporosis, off-label BPs require informed consent. Children most frequently use second- and third-generation BPs. Others are administered orally, while some are intravenously. Adult osteoporosis is frequently treated with oral BPs, and some studies have shown that these drugs increase BMD and reduce fracture risk in those with Osteogenesis Imperfecta. They shouldn't be utilised on people who have esophagitis risk factors such gastro-esophageal reflux disease or hiatal hernia because they can't reconstruct the oesophagus after VF like intravenous BPs can. When intravenous distribution is prohibited or during treatment maintenance, intravenous BPs are superior to oral BPs for treating moderate osteoporosis without VF [36].

Anabolic: Low bone turnover is a common feature of several types of pediatric osteoporosis, such as osteoporosis brought on by neuromuscular abnormalities and glucocorticoid exposure. Anti-resorptive medication in these situations further reduces bone turnover with possible hazards, which has raised attention to anabolic medicines [12].

Growth Hormone (GH): In youngsters who lack it, GH enhances bone mineral content by increasing muscle area, the strength-strain index, and bone geometry. In the first six months of treatment, GH only modestly improved bone density in the lumbar spine (5–7%), therefore it did not lower fracture rates or increase bone density in children with OI. Because the data does not support the use of GH alone to treat osteoporosis, treatment should be restricted to the suggested circumstances [12].

Anti-Sclerostin Antibodies: Sclerostin, which is released by osteoclasts and inhibits Wnt signaling and bone formation by interacting with LRP5 and LRP6 receptors. Anti-sclerostin antibodies boost bone synthesis in postmenopausal women and mice, but the benefit disappears and bone loss occurs if treatment is stopped. Anti-resorptive drugs can stop this after the anti-sclerostin antibodies are stopped. BPS804 anti-sclerostin antibody boosts bone formation, lowers bone resorption, and improves aBMD in people with mild OI, according to Glorieux et al.'s findings in a phase IIa rganizati trial. The outcomes of a paediatric trial have not yet been released [12].

Whole Body Vibration Therapy (WBV): WBV therapy helps adolescents with CP and other teenage crippling illnesses walk faster, have stronger muscles, are less stiff, and have better balance, according to tiny rganizati controlled trials and observational studies. The mechanostat theory is the foundation for the WBV treatment for osteoporosis. When bone density was the primary goal of the study, it was shown that "low-magnitude" vibration was less beneficial than bisphosphonate medication. The study participants were young children with Crohn's disease. WBV enhanced lean mass in children with OI without changing muscular strength or bone density, indicating a reduced biomechanical interaction between the muscle and bone units [12].

Follow-Up

Candidates for treatment are found through monitoring for risk factors for osteoporosis. These patients, as well as those who have a verified diagnosis, should get follow-up care as long as risk factors continue to exist or calcium, vitamin D, BPs, or other osteoporosis medications are continued [36].

Clinical, radiological, and analytical data need monitoring. Counting pain and fragility fractures is key. Z-scores affect densitometry. DXA performance frequency is unclear. Clinicians recommend repeating DXA after a year, then every 1-2 years depending on the patient's trajectory, with a minimum delay of 6–12 months [36]. Calciuria and plasmatic 25-hydroxyvitamin D3 and iPTH values should be used to rganiza calcium and vitamin D supplement doses for kids and teens with chronic diseases since the optimal intake is unknown. Some writers suggest testing these traits every 3–12 months, but the best period is undetermined. Medical rganization recommends monitoring 25-hydroxyvitamin D3 levels every 6–12 months or 3–6 months after a dose change. Calciuria should be tested annually. To rule out nephrocalcinosis, a renal ultrasonography should be done when calciuria rises or urine collection fails. Analytical testing frequency in BP-treated children has not been studied. Monitor intravenous BPs before each infusion, and oral BPs every six months [36].

Specific Disorders Resulting In Osteoporosis In Children

Cerebral Palsy: A non-progressive encephalopathy characterized by abnormal mobility and posture, is what we call CP. According to several reports, the prevalence of fractures in children with CP ranges from 5-30%, with most of fractures happening in the femoral shaft and supracondylar region [37]. In children with CP, decreased movement is the main factor contributing to bone fragility. Reduced mobility causes bones to have low bone mass, an atypical architectural design, and to be less able to tolerate mechanical difficulties such powerful muscular contractions brought on by convulsions or extraordinary weight bearing or transfer. Other factors include nutritional problems, disorders of puberty, vitamin D inadequacy brought on by less sunlight exposure, and perhaps anti-convulsant medication. With the exception of more severely affected children whose spine is also impacted, lumbar spine BMD is frequently regular in CP children who experience a pathological fracture [38]. For the kid with CP, additional general measures like providing enough calcium and vit D consumption, nutrition, reducing induced causes of bone loss, and supporting puberty growth are also crucial. When osteoporosis is confirmed, bisphosphonate medication is appropriate [39].

Leukemia: Childhood cancer is dominated by leukaemia. The two most significant skeletal effects of leukaemia are osteoporosis and AVN. Children with acute lymphoblastic leukaemia had a 28% cumulative fracture incidence over a five-year period, according to Strauss et al. In acute lymphoblastic leukaemia, skeletal issues are linked to the use of glucocorticoids, malnutrition, immobility, methotrexate, cranial irradiation, poor bone mineralization, older age at diagnosis, and male sex. Children with leukaemia who also have hypothyroidism, insufficient growth hormone, and hypogonadism may have weak bones [1].

Children with intellectual disabilities: Intellectually impaired children risk osteoporosis. Low BMD, osteoporosis, and osteopenia are prevalent in this population. Ageing, anticonvulsants, mobility, and Down's syndrome lower BMD. The majority of studies revealed that individuals with cognitive impairment have more than two risk factors. Anticonvulsants (64%) were listed as osteoporosis risk factors, along with mobility (23%) and falls (20%) and fractures (11%). For those who are intellectually challenged, BMD testing is necessary. To reduce morbidity and enhance quality of life, more research should be conducted and individuals with osteopenia and osteoporosis should receive early treatment [40].

Conclusion

Osteoporosis is a major childhood health issue that can either be the main disorder or a sequel to a chronic illness. Children with osteoporosis should meet with or be referred to a pediatric bone expert. The doctor must adopt a comprehensive plan for the prevention and treatment of bone disease because there are plentiful factors that might affect the bone health of youngsters. In addition to bisphosphonate therapy, dietary, hormonal, and biomechanical therapeutic regimens are required. This strategy and ongoing research may make it possible to enhance children's general wellbeing, the quality of their future adult lives, and their quality of life as they age. To date, DXA, radiography, and pQCT are the modalities of best choice for assessing bone health and diagnosing VFs. Research on childhood osteoporosis is still in its infancy.

Conflict of Interest

None

Funding

None

References

1. Khoshhal KI. Childhood osteoporosis. Journal of Taibah University Medical Sciences. 2011;6(2):61-76.
2. Gordon CM, Zemel BS, Wren TA, Leonard MB, Bachrach LK, Rauch F, et al. The determinants of peak bone mass. The Journal of pediatrics. 2017;180:261-269.
3. Santos L, Elliott-Sale KJ, Sale C. Exercise and bone health across the lifespan. Biogerontology. 2017;18:931-946.
4. Rizzoli R, Bianchi ML, Garabédian M, McKay HA, Moreno LA. Maximizing bone mineral mass gain during growth for the prevention of fractures in the adolescents and the elderly. Bone. 2010;46(2):294-305.
5. Clynes MA, Harvey NC, Curtis EM, Fuggle NR, Dennison EM, Cooper C. The epidemiology of osteoporosis. British medical bulletin. 2020;133(1), 105–117.
6. Clark EM. The epidemiology of fractures in otherwise healthy children. Current osteoporosis reports. 2014;12:272-278.
7. Bishop N, Arundel P, Clark E, Dimitri P, Farr J, Jones G, et al. Fracture prediction and the definition of osteoporosis in children and adolescents: the ISCD 2013 Pediatric Official Positions. Journal of Clinical Densitometry. 2014;17(2):275-280.
8. Ward LM, Weber DR, Munns CF, Högler W, Zemel BS. A Contemporary View of the Definition and Diagnosis of Osteoporosis in Children and Adolescents. J Clin Endocrinol Metab. 2020;105(5):e2088-e2097.

9. Ronne MS, Heidemann M, Schou A, Laursen JO, Bojesen AB, Lylloff L, et al. Tracking of bone mass from childhood to puberty: a 7-year follow-up. The CHAMPS study DK. Osteoporosis International. 2018;29:1843-1852.
10. Arundel P, Bishop N. Primary osteoporosis. Endocr Dev 2015;28:162–175.
11. Presedo A, Dabney KW, Miller F. Fractures in patients with cerebral palsy. Journal of Pediatric Orthopaedics. 2007;27(2):147-153.
12. Glorieux FH, Devogelaer JP, Durigova M, et al. BPS804 Anti-Sclerostin Antibody in Adults With Moderate Osteogenesis Imperfecta: Results of a Randomized Phase 2a Trial. J Bone Miner Res. 2017;32(7):1496-1504. doi:10.1002/jbmr.3143
13. Clarke B. Normal bone anatomy and physiology. Clinical journal of the American Society of Nephrology. 2008;3(Supplement 3):S131-139.
14. Tzaphlidou M, Berillis P. Collagen fibril diameter in relation to bone site. A quantitative ultrastructural study. Micron. 2005;36(7-8):703-705.
15. Ciancia S, van Rijn RR, Högler W, Appelman-Dijkstra NM, Boot AM, Sas TC, et al. Osteoporosis in children and adolescents: when to suspect and how to diagnose it. European journal of pediatrics. 2022;181(7):2549-2561.
16. Ward LM, Konji VN, Ma J. The management of osteoporosis in children. Osteoporos Int. 2016;27(7):2147-2179.
17. Huber AM, Gaboury I, Cabral DA, et al. Prevalent vertebral fractures among children initiating glucocorticoid therapy for the treatment of rheumatic disorders. Arthritis Care Res (Hoboken). 2010;62(4):516-526.
18. Verwaaijen EJ, Ma J, de Groot-Kruseman HA, et al. A Validated Risk Prediction Model for Bone Fragility in Children with Acute Lymphoblastic Leukemia. J Bone Miner Res. 2021;36(12):2290-2299.
19. Weber DR, Thomas S, Erickson SW, et al. Bone Health and Endocrine Care of Boys with Duchenne Muscular Dystrophy: Data from the MD STARnet. J Neuromuscul Dis. 2018;5(4):497-507.
20. Tantawy AA, El Bostany EA, Matter RM, El Ghoroury EA, Ragab S, El Sherif NH. Bone mass and biochemical markers of bone turnover in children and adolescents with chronic immune thrombocytopenia: relation to corticosteroid therapy and vitamin D receptor gene polymorphisms. Platelets. 2013;24(4):282-287.
21. Formosa MM, Bergen DJ, Gregson CL, Maurizi A, Kämpe A, Garcia-Giralt N, et al. A roadmap to gene discoveries and novel therapies in monogenic low and high bone mass disorders. Frontiers in Endocrinology. 2021;12:709711.
22. Crabtree NJ, Arabi A, Bachrach LK, et al. Dual-energy X-ray absorptiometry interpretation and reporting in children and adolescents: the revised 2013 ISCD Pediatric Official Positions. J Clin Densitom. 2014;17(2):225-242.
23. Zemel BS, Stallings VA, Leonard MB, Paulhamus DR, Kecskemethy HH, Harcke HT, et al. Revised pediatric reference data for the lateral distal femur measured by Hologic Discovery/Delphi dual-energy X-ray absorptiometry. Journal of Clinical Densitometry. 2009;12(2):207-218.
24. Ward LM, Hadjiyannakis S, McMillan HJ, Noritz G, Weber DR. Bone Health and Osteoporosis Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics. 2018;142(Suppl 2):S34-S42.
25. Subramaniam K, Babu T. Does Bone Mineral Apparent Density Facilitate Accurate Identification of Osteoporosis in the Short Postmenopausal Women. Indian J Endocrinol Metab. 2020;24(3):275-279.
26. Zemel BS, Kalkwarf HJ, Gilsanz V, Lappe JM, Oberfield S, Shepherd JA, et al. Revised reference curves for bone mineral content and areal bone mineral density according to age and sex for black and non-black children: results of the bone mineral density in childhood study. The Journal of Clinical Endocrinology & Metabolism. 2011;96(10):9-3160.
27. Alqahtani FF, Offiah AC. Diagnosis of osteoporotic vertebral fractures in children. Pediatric radiology. 2019;49:283-296.
28. Wáng YX, Santiago FR, Deng M, Nogueira-Barbosa MH. Identifying osteoporotic vertebral endplate and cortex fractures. Quantitative imaging in medicine and surgery. 2017;7(5):555.
29. Malgo F, Hamdy NAT, Ticheler CHJM, et al. Value and potential limitations of vertebral fracture assessment (VFA) compared to conventional spine radiography: experience from a fracture liaison service (FLS) and a meta-analysis. Osteoporos Int. 2017;28(10):2955-2965.
30. Binkley T, Johnson J, Vogel L, Kecskemethy H, Henderson R, Specker B. Bone measurements by peripheral quantitative computed tomography (pQCT) in children with cerebral palsy. The Journal of pediatrics. 2005;147(6):791-796.
31. Högler W, Shaw N. Childhood growth hormone deficiency, bone density, structures and fractures: scrutinizing the evidence. Clinical endocrinology. 2010;72(3):281-289.
32. Rauch F, Plotkin H, Travers R, Zeitlin L, Glorieux FH. Osteogenesis imperfecta types I, III, and IV: effect of pamidronate therapy on bone and mineral metabolism. J Clin Endocrinol Metab. 2003;88(3):986–992.
33. Ward LM, Rauch F, Matzinger MA, Benchimol EI, Boland M, Mack DR. Iliac bone histomorphometry in children with newly diagnosed

inflammatory bowel disease. Osteoporos Int. 2010;21(2):331–337.
34. Bachrach LK, Ward LM. Clinical review 1: Bisphosphonate use in childhood osteoporosis. J Clin Endocrinol Metab. 2009;94:400–409.
35. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al., Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96:1911–1930.
36. Galindo-Zavala R, Bou-Torrent R, Magallares-López B, et al. Expert panel consensus recommendations for diagnosis and treatment of secondary osteoporosis in children. Pediatr Rheumatol Online J. 2020;18(1):20.
37. Ward L, Glorieux FH. The Spectrum of Pediatric Osteoporosis. In: Glorieux FH, Pettifor J, Jueppner H (eds) Pediatric Bone: Biology and Disease. San Diego, Academic Press. 2003;401- 442.
38. Wren TA, Lee DC, Kay RM, Dorey FJ, Gilsanz V. Bone density and size in ambulatory children with cerebral palsy. Dev Med Child Neurol. 2011; 53(2): 137- 141.
39. Munns CFJ, Cowell CT. Prevention and treatment of osteoporosis in chronically ill children. J Musculoskelet Neuronal Interact. 2005; 5(3): 262-272.
40. Srikanth R, Cassidy G, Joiner C, Teeluckdharry S. Osteoporosis in people with intellectual disabilities: a review and a brief study of risk factors for osteoporosis in a community sample of people with intellectual disabilities. J Intellect Disabil Res. 2011; 55(1): 53-62.