IJBPAS, August, Special Issue, 2021, 10(8): 409-422

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

AWARENESS ON RICKETS AND OSTEOMALACIA AMONG COLLEGE STUDENTS

ANANYA R[1], VISHNU PRIYA V[2] AND GAYATHRI. R[3]

1: Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS) Saveetha University, Chennai- 600077

2: Department of Biochemistry, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai-600077

3: Department of Biochemistry, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS) Saveetha University, Chennai-600077

***Corresponding Author: E Mail: Dr. Vishnu Priya V: vishnupriya@saveetha.com**

Received 19th March 2021; Revised 20th April. 2021; Accepted 19th May 2021; Available online 1st Aug. 2021

https://doi.org/10.31032/IJBPAS/2021/10.8.1030

ABSTRACT

Osteomalacia is a common disorder which occurs due to impaired mineralisation of osteoid, whereas rickets occurs due to impaired mineralisation of cartilaginous growth plates. Since adults have fused growth plates they are only affected by osteomalacia. In childrens whose growth plates are open, the disorder can occur simultaneously. The most common cause for both these disorders is vitamin D deficiency resulting due to inadequate intake, malabsorption or lack of exposure to sunlight. The aim is to create awareness about rickets and osteomalacia among the college students. A questionnaire was prepared using Google forms based on the awareness of rickets and osteomalacia. It was then circulated among college students using applications such as Whatsapp and Gmail. The results were then calculated and presented with accurate statistics. 64% of students are aware of rickets and osteomalacia and 36% of them are unaware. According to the results, we can understand that most of the college students have a basic knowledge about rickets and osteomalacia, but they are unaware about the major difference between them and the

preventive measures and treatment. Health education camps, seminars, workshops may be conducted to create awareness on risk factors, complications, treatment for rickets and osteomalacia for the community.

Keywords : Osteomalacia, rickets, Vitamin D, Vitamin D deficiency, Vitamin D dependent rickets

INTRODUCTION

The incidence of nutritional disorders have increased globally. Rickets and osteomalacia being the most commonly occurring nutritional disorders, where rickets occur due to impaired mineralisation of cartilaginous growth plates and osteomalacia occurs due to impaired mineralisation of osteoid **[1]**. In children whose growth plates are open, the disorders can occur simultaneously **[1]**. The basic mechanism in all forms of rickets is low serum phosphate resulting in decreased apoptosis of hypertrophic chondrocytes in the growth plate and decreased mineralisation of primary spongiosa in the metaphysis (new bone) **[2]**. Osteomalacia contains defective mineralisation of the existing bones (old bones) during the remodelling process. Therefore, osteomalacia is not just a disorder that occurs in adults, but the main reason for the occurrence of long bone bowing deformities and fractures in children with rickets due to poor mineralisation which reduces bone stiffness **[3]**. Low calcium intake and or low vitamin D are the leading causes of calcium deprivation and also their combined deficiency causes bone demineralisation **[4]**. This calcium deprivation not only causes bone demineralisation but can also lead to hypocalcemic seizures, tetany and dilated cardiomyopathy including cardiac failure and death **[5, 6]**. Public health research has identified traditional diets which are low in calcium, dark skin and cultural full body clothing, as a main causes of rickets and osteomalacia in sunny parts of the world such as the Indian subcontinent **[7]**, the Middle East **[8]** and Africa **[9]**. In high Northern or Southern latitudes (more than approximately 34°), it is the seasonal lack of the ultraviolet-B (UV-B) spectrum of sunlight that causes seasonal vitamin D deficiency (also called 'vitamin D winter') **[10]**. In high latitude countries, the dark-skinned immigrant and resident population is at greatest risk **[8, 10]**. Vitamin D (calciferol) is produced in human skin (D3) following exposure to UV-B light, or consumed with food (D2 and D3), then transferred in the liver to 25-hydroxyvitamin D (25OHD, calcidiol) and resulting in the kidney and also in the gut **[8,10,11]** to the active hormone $1,25(OH)_2D$

(calcitriol or 'active vitamin D'). Calcium and phosphate are considered as the most important mineral ions which are responsible for the bone stiffness **[12]**. Calcitriol being the principle supplier of these bone minerals, which are absorbed regularly, by enlarging their intestinal absorption. Hence calcitriol cannot do its job in individuals with no oral intake **[13]**. Reduced dietary calcium supply and vitamin D status can lead to calcium deprivation, which is immediately analysed by the calcium sensing receptor present in the parathyroid's chief cells, resulting in more release of parathyroid hormone (PTH) **[14]**. This secondary hyperparathyroidism triggers osteoclastic bone resorption with the intention to release stored bone minerals. This alternate mechanism works well to maintain normal serum calcium levels, but prolonged hyperparathyroidism has two main difficulties: (1) structural damage to bone and (2) reduced renal reabsorption of phosphate **[14-16]**. The 'Ideal' serum 25OHD concentration remains debatable, with definitions varying from >50 to >100 nmol/L (20 to 40 μg/L). All children with rickets are to be treated with vitamin D for a minimum of 3 months with a daily dose of at least 2000 IU (50 μg) if aged <12 months, 3000–6000 IU (50–150 μg) if aged 12 months–12 years, and 6000 IU (150 μg) if aged >12 years **[17]**, **[18]** Single high dose (Stoss therapy) can be used in resource-limited settings in infants aged >3 months: 50,000 IU (1250 μg) for 3 months–12 months of age, 150,000 IU (3750 μg) for children aged 12 months–12 years, and 300,000 IU (7500 μg) if aged >12 years **[19]**. All individuals should also receive concomitant calcium (minimum 500 mg/day) as supplements or via diet. All treatment should be followed by lifelong vitamin D supplements, since the underlying risk (ethnicity, culture and sunlight exposure) is unlikely to change **[20]**. NR and osteomalacia are completely preventable. Universal supplementation of infants , supplementing pregnant women , promoting vitamin uptake and also food defence with vitamin D and calcium to avoid fractures in elderly have been proven cost-effective **[21]**. Previously our team has a rich experience in working on various research projects across multiple disciplines **[22–36]**. The aim of this study is to create awareness about rickets and osteomalacia among the college students.

MATERIALS AND METHODS

This questionnaire based survey was designed based on the awareness of rickets and osteomalacia. The questionnaire was administered through an online survey link to the college students. The study was approved

by the Institutional Review Board, Saveetha Dental College. The participants were well explained about the study and responses were collected. The data collected was statistically analysed. The output variables were represented as pie charts.

RESULTS AND DISCUSSION

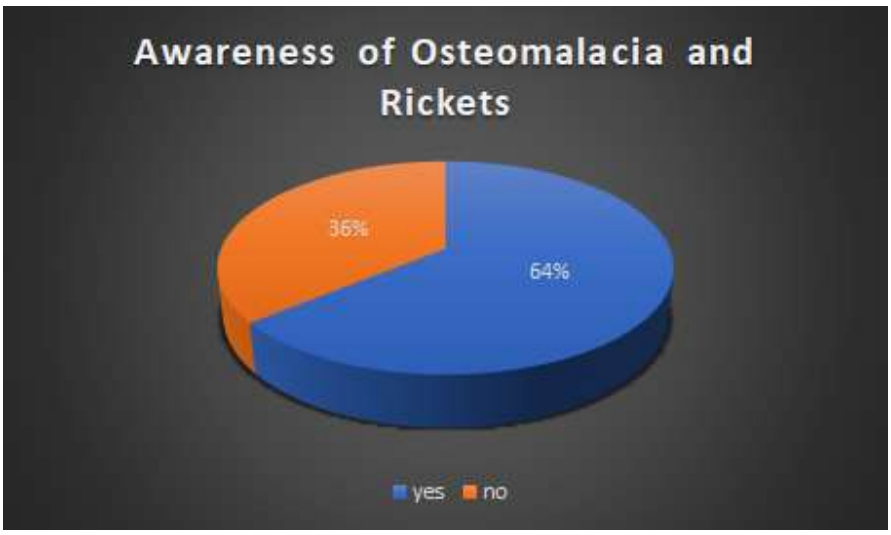

Figure 1: Pie chart represents the percentage distribution of responses about awareness on osteomalacia and rickets. .64% of them are aware of osteomalacia and rickets, 36% of them unaware of osteomalacia and rickets

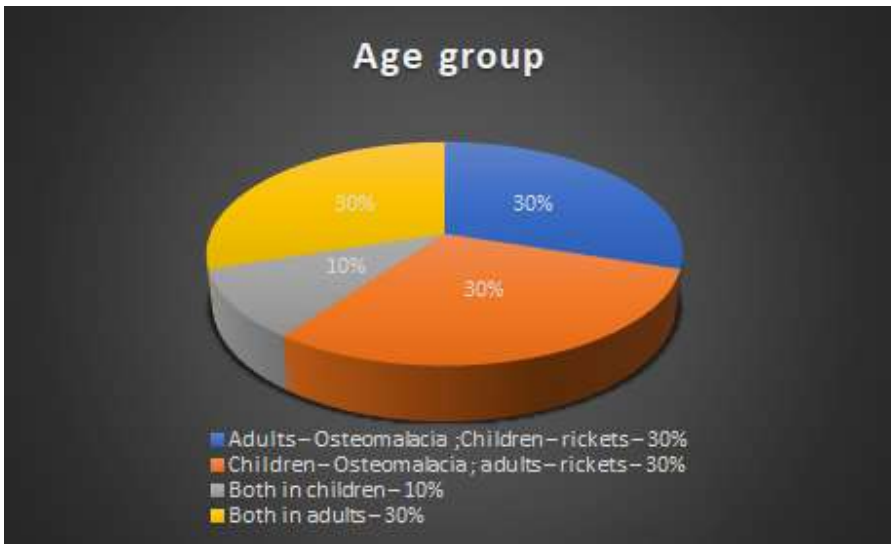

Figure 2: Pie chart represents the percentage distribution of responses to disorder which occurs in adults and children. Only 30% of them chose Adults – Osteomalacia ;Children – rickets, 30% of them chose Children – Osteomalacia ; adults – rickets, 10% of them thought both occurs in children and around 30% of them thought both occurs in adults.

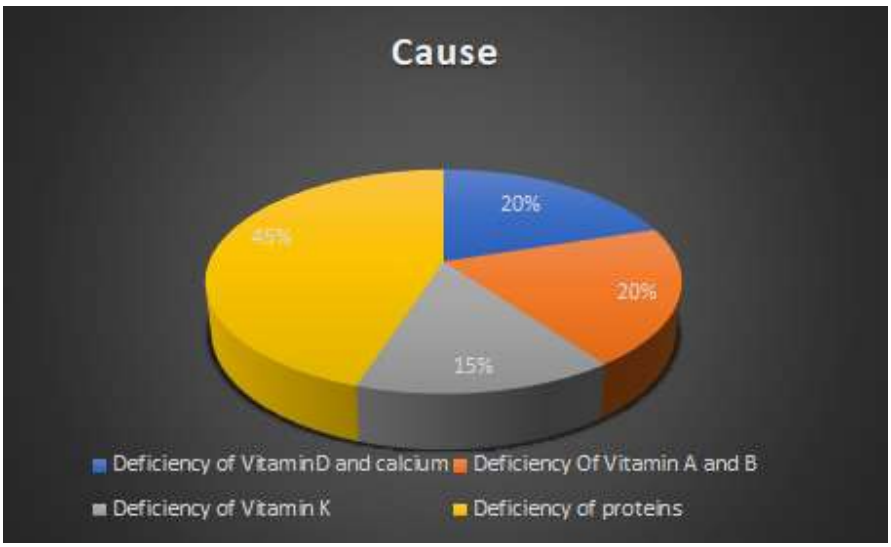

Figure 3: Pie chart represents the percentage distribution of responses to the reason for the occurrence rickets and osteomalacia. 20% of them state it is due to the deficiency of vitamin D and calcium, 20% of them state it is due to the deficiency Of Vitamin A and B, 15% of them state it is due to the deficiency Of Vitamin K ,45% of them state it is due to the deficiency of proteins

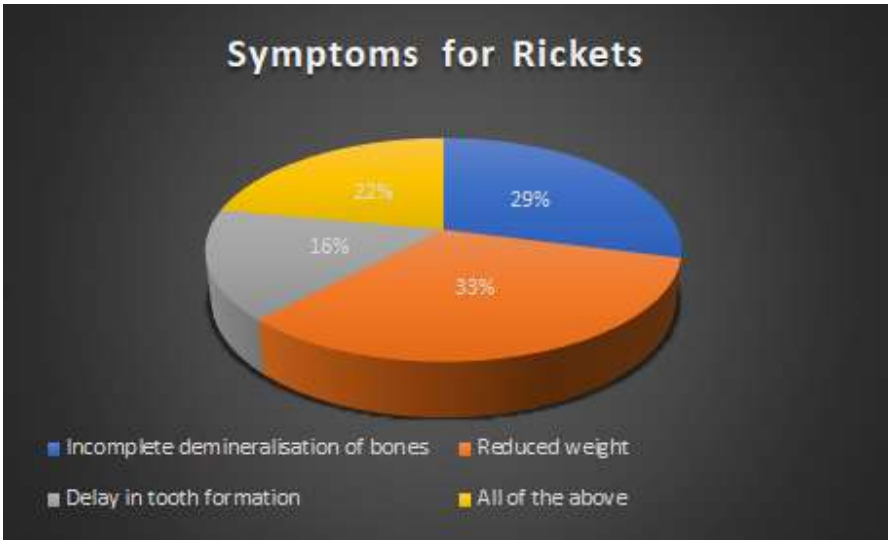

Figure 4: Pie chart represents the percentage distribution of responses to symptoms for Rickets. 29% of them state that the symptom is incomplete demineralisation of bones 33% of them state it is reduced weight, 16% of them state it is delay in tooth forms, 22% of them state it is the all the symptoms mentioned above.

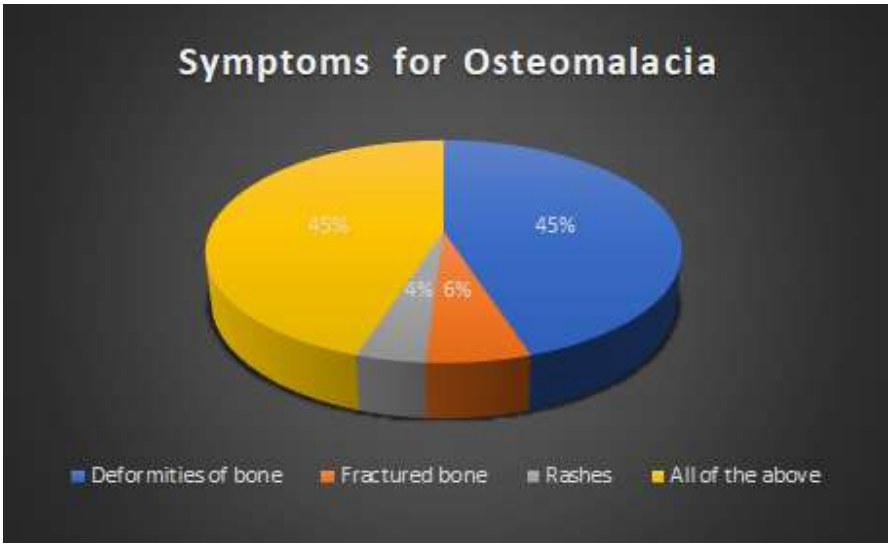

Figure 5: Pie chart represents the percentage distribution of responses to symptoms for Osteomalacia. 45% of them state that the symptom is deformities of bone, 6% of them state it is fractured bone, 4% of them state it is rashes,45% of them state it is all the symptoms mentioned above.

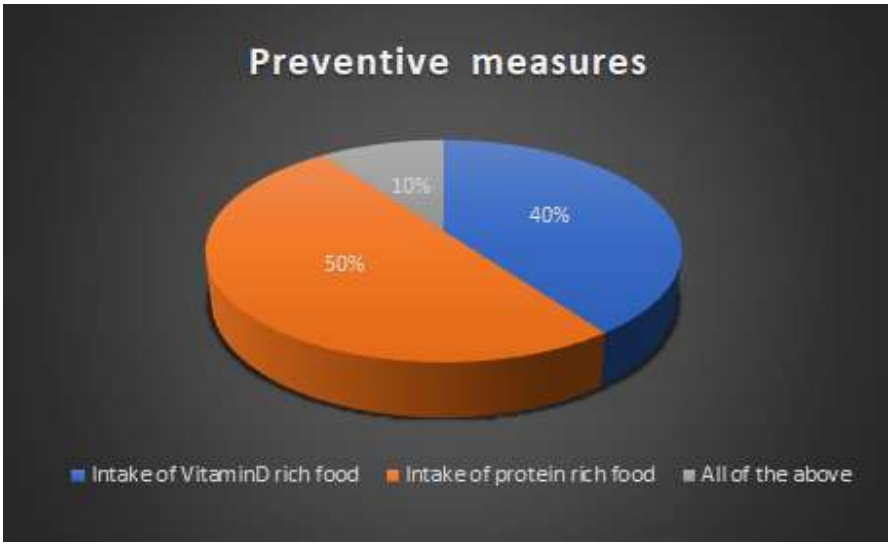

Figure 6: Pie chart represents the percentage distribution of responses to preventive measures taken. 40% of them state that intake of vitamin D rich foods, 50% of them state it is intake of protein rich foods, 10% of them state it is all the preventive measures mentioned above

From the above results we can see that, among the total number of participants, only 64% of them are aware of osteomalacia and rickets disorder in which 36% are completely unaware of the disorders (**Figure 1**). Rickets are a major issue even in countries with sufficient access to the sun. The causes of rickets / osteomalacia are varied and include nutritional deficiencies, particularly low vitamin D and calcium intakes. Non-nutritional causes include hypophosphatemic rickets mainly due to loss of renal phosphate and rickets due to acidosis of the renal tubules **[37]**. When asked about the age group in which these both occur, only 30% of them knew that osteomalacia occurs in adults

and rickets in children other 30% of them thought osteomalacia occurs in children and rickets in adults which is false. The other 30% stated that both occur in adults which is again false, and the remaining 10% of students stated that both occur in children which is again false statement. From this we can analyse that students are not aware of the age group of occurrence itself, which they might get a clear idea from this study **(Figure 2)**. Any child who is not getting enough vitamin D or calcium from their diet, or from sunlight, can develop rickets. But the disorder is more common in children with dark skin, because this means they need more sunshine to get enough vitamin D, as well as children born prematurely or on vitamin D-interfering drugs **[38]**. Moving on to the causes of these disorders , among the total population only 20% of them stated that it is due to the deficiency of vitamin D and calcium, other 20% of them believed that it is due to the deficiency of vitamin A and B , 15% of them thought it is due to deficiency of vitamin K and around 45% of them think it is due to deficiency of proteins which is a false assumption **(Figure 3)**. The most common cause of both osteomalacia and rickets is a deficiency of vitamin D caused by insufficient consumption, malabsorption or lack of sunlight exposure. Osteomalacia patients typically have bone pain and tenderness, while ricket patients exhibit bone deformities and impaired development **[39]**. In **Figure 4** we can observe that, 29% of the students think that demineralisation of bones is the main symptom for rickets, 33% of them state that reduction of weight is the symptom, 16% of them think there will be delay in tooth formation as a symptom of rickets and 22% of them state that all of the above symptoms occur in a rickets patient. Rickets are most often caused by a lack of vitamin D or calcium in a child's diet. These are important for the production of strong and healthy bones in children. Vitamin D sources are: sunlight-your skin produces vitamin D when exposed to the sun, and this way we get most of our vitamin D **[40]**. In case of symptoms of osteomalacia, 45% of them state that deformities in the bone can be noticed as a symptom , 6% of them think fracturing of bones might occur as a symptom , 4% - rashes and 45% of them think all the above symptoms can occur (**Figure 5**). Osteomalacia results from a mistake in the cycle of bone maturing. The minerals calcium and phosphate are used in the body to help create solid bones **[41]**. In **Figure 6** we can see that only 40% of them are aware of the correct preventive measure for osteomalacia and rickets which is intake

of vitamin D rich foods , but majority of the students that is around 50% of them state that intake of proteins might help from osteomalacia and rickets and 10% of them think that both consumption of vitamin D and proteins will help be a good preventive measure. Those include supplying your child with a healthy, balanced diet, spending some time out in the sun, taking a supplement of vitamin D. Babies from birth to one year, including those that are breastfed fully or partially, require 8.5 to 10 micrograms (mcg) of vitamin D per day. Children 1 year old and adults need 10mcg of vitamin D a day **[42]**. From the above analysis we can say that people are aware of osteomalacia and rickets but are unaware of their main differences. A very few of them are aware that deficiency of vitamin D and calcium is the major cause for the occurrence of both the disorders because for normal bone growth and mineralisation calcium is required, and also students mainly are unaware about which specific age group of people are affected by these disorders. Our institution is passionate about high quality evidence based research and has excelled in various fields **[43–49]**. We hope this study adds to this rich legacy.

CONCLUSION

According to the results, we can understand that most of the college students have a basic knowledge about rickets and osteomalacia, but they are unaware about the major difference between them and the preventive measures and treatment. Since osteomalacia and rickets being an important deficiency, occurred mainly due to their lack of knowledge about it, which can be prevented in early stages with good diet intake like vitamin D rich foods. Hence this study may help them gain some more clear basic knowledge about osteomalacia and rickets. Health education camps, seminars, workshops may be conducted to create awareness on risk factors, complications, treatment for rickets and osteomalacia for the community.

ACKNOWLEDGEMENT

The authors thank Saveetha Dental College for extending full support to complete this study.

CONFLICT OF INTEREST: Nil

REFERENCES

[1] Prentice A. Nutritional rickets around the world. J Steroid Biochem Mol Biol. 2013 Jul;136:201–6.

[2] Goldacre M, Hall N, Yeates DGR. Hospitalisation for children with rickets in England: a historical perspective [Internet]. Vol. 383, The Lancet. 2014. p. 597–8. Available from:

http://dx.doi.org/10.1016/s0140-6736(14)60211-7

[3] Ahmed SF, Franey C, McDevitt H, Somerville L, Butler S, Galloway P, *et al*. Recent trends and clinical features of childhood vitamin D deficiency presenting to a children's hospital in Glasgow [Internet]. Vol. 96, Archives of Disease in Childhood. 2011. p. 694–6. Available from: http://dx.doi.org/10.1136/adc.2009.173195

[4] Högler W. Complications of vitamin D deficiency from the foetus to the infant: One cause, one prevention, but who's responsibility? [Internet]. Vol. 29, Best Practice & Research Clinical Endocrinology & Metabolism. 2015. p. 385–98. Available from: http://dx.doi.org/10.1016/j.beem.2015.03.003

[5] Sanyal D, Raychaudhuri M. Infants with dilated cardiomyopathy and hypocalcemia. Indian J Endocrinol Metab. 2013 Oct;17(Suppl 1):S221–3.

[6] Maiya S, Sullivan I, Allgrove J, Yates R, Malone M, Brain C, *et al.* Hypocalcaemia and vitamin D deficiency: an important, but preventable, cause of life-threatening infant heart failure. Heart. 2008 May;94(5):581–4.

[7] Basatemur E, Sutcliffe A. Incidence of Hypocalcemic Seizures Due to Vitamin D Deficiency in Children in the United Kingdom and Ireland [Internet]. Vol. 100, The Journal of Clinical Endocrinology & Metabolism. 2015. p. E91–5. Available from: http://dx.doi.org/10.1210/jc.2014-2773

[8] Priemel M, von Domarus C, Klatte TO, Kessler S, Schlie J, Meier S, *et al.* Bone mineralization defects and vitamin D deficiency: Histomorphometric analysis of iliac crest bone biopsies and circulating 25-hydroxyvitamin D in 675 patients [Internet]. Vol. 25, Journal of Bone and Mineral Research. 2010. p. 305–12. Available from: http://dx.doi.org/10.1359/jbmr.090728

[9] Scheimberg I, Perry L. Does Low Vitamin D Have a Role in Pediatric Morbidity and Mortality? An Observational Study of Vitamin D in a Cohort of 52 Postmortem Examinations [Internet]. Vol. 17, Pediatric and Developmental

Pathology. 2014. p. 455–64. Available from: http://dx.doi.org/10.2350/14-05-1491-oa.1

[10] Cohen MC, Offiah A, Sprigg A, Al-Adnani M. Vitamin D deficiency and sudden unexpected death in infancy and childhood: a cohort study. Pediatr Dev Pathol. 2013 Jul;16(4):292–300.

[11] Cashman KD, Dowling KG, Škrabáková Z, Gonzalez-Gross M, Valtueña J, De Henauw S, *et al.* Vitamin D deficiency in Europe: pandemic? Am J Clin Nutr. 2016 Apr;103(4):1033–44.

[12] Thacher TD, Pludowski P, Shaw NJ, Mughal MZ, Munns CF, Högler W. Nutritional rickets in immigrant and refugee children. Public Health Rev. 2016 Jul 22;37:3.

[13] Munns CF, Shaw N, Kiely M, Specker BL, Thacher TD, Ozono K, *et al.* Global Consensus Recommendations on Prevention and Management of Nutritional Rickets [Internet]. Vol. 85, Hormone Research in Paediatrics. 2016. p. 83–106. Available from: http://dx.doi.org/10.1159/000443136

[14] Julies P, Pall K, Lynn R, Calder A, Mughal MZ, Shaw NJ, *et al.* OC-73 Nutritional rickets presenting to secondary care in children (<16 years) – a uk surveillance study [Internet]. Oral Communications. 2017. Available from: http://dx.doi.org/10.1136/archdischild-2017-313273.73

[15] Glorieux FH, Pettifor JM, Jüppner H. Pediatric Bone: Biology and Diseases. Gulf Professional Publishing; 2003. 758 p.

[16] Tiosano D, Hochberg Z 'ev. Hypophosphatemia: the common denominator of all rickets. J Bone Miner Metab. 2009 Jun 6;27(4):392–401.

[17] Aggarwal V, Seth A, Aneja S, Sharma B, Sonkar P, Singh S, *et al*. Role of calcium deficiency in development of nutritional rickets in Indian children: a case control study. J Clin Endocrinol Metab. 2012 Oct;97(10):3461–6.

[18] de Pee S, Taren D, Bloem MW. Nutrition and Health in a Developing World. Humana Press; 2017. 827 p.

[19] Hochberg Z. Vitamin D and Rickets. Karger Medical and Scientific

Publishers; 2003. 291 p.

[20] Hassan N. The Chakaria Food System Study: A Household-level, Case-control Study to Identify Risk Factors for Rickets. 2002. 64 p.

[21] Glorieux FH, Pettifor JM, Jüppner H. Pediatric Bone: Biology & Diseases. Academic Press; 2012. 853 p.

[22] Neelakantan P, Sharma S, Shemesh H, Wesselink PR. Influence of Irrigation Sequence on the Adhesion of Root Canal Sealers to Dentin: A Fourier Transform Infrared Spectroscopy and Push-out Bond Strength Analysis. J Endod. 2015 Jul;41(7):1108–11.

[23] Sathish T, Karthick S. Wear behaviour analysis on aluminium alloy 7050 with reinforced SiC through taguchi approach. J Jpn Res Inst Adv Copper-Base Mater Technol. 2020 May;9(3):3481–7.

[24] Patil SB, Durairaj D, Suresh Kumar G, Karthikeyan D, Pradeep D. Comparison of Extended Nasolabial Flap Versus Buccal Fat Pad Graft in the Surgical Management of Oral Submucous Fibrosis: A Prospective Pilot Study. J Maxillofac Oral Surg. 2017 Sep;16(3):312–21.

[25] Abdul Wahab PU, Senthil Nathan P, Madhulaxmi M, Muthusekhar MR, Loong SC, Abhinav RP. Risk Factors for Post-operative Infection Following Single Piece Osteotomy. J Maxillofac Oral Surg. 2017 Sep;16(3):328–32.

[26] Eapen BV, Baig MF, Avinash S. An Assessment of the Incidence of Prolonged Postoperative Bleeding After Dental Extraction Among Patients on Uninterrupted Low Dose Aspirin Therapy and to Evaluate the Need to Stop Such Medication Prior to Dental Extractions. J Maxillofac Oral Surg. 2017 Mar;16(1):48–52.

[27] Wahab PUA, Madhulaxmi M, Senthilnathan P, Muthusekhar MR, Vohra Y, Abhinav RP. Scalpel Versus Diathermy in Wound Healing After Mucosal Incisions: A Split-Mouth Study. J Oral Maxillofac Surg. 2018 Jun;76(6):1160–4.

[28] Jeevanandan G, Govindaraju L. Clinical comparison of Kedo-S paediatric rotary files vs manual instrumentation for root canal preparation in primary molars: a double blinded randomised clinical trial [Internet]. Vol. 19, European

Archives of Paediatric Dentistry. 2018. p. 273–8. Available from: http://dx.doi.org/10.1007/s40368-018-0356-6

[29] Samuel SR, Acharya S, Rao JC. School Interventions-based Prevention of Early-Childhood Caries among 3-5-year-old children from very low socioeconomic status: Two-year randomized trial. J Public Health Dent. 2020 Jan;80(1):51–60.

[30] Mehta M, Deeksha, Tewari D, Gupta G, Awasthi R, Singh H, *et al*. Oligonucleotide therapy: An emerging focus area for drug delivery in chronic inflammatory respiratory diseases. Chem Biol Interact. 2019 Aug 1;308:206–15.

[31] Ezhilarasan D, Sokal E, Najimi M. Hepatic fibrosis: It is time to go with hepatic stellate cell-specific therapeutic targets. Hepatobiliary Pancreat Dis Int. 2018 Jun;17(3):192–7.

[32] Rajeshkumar S, Menon S, Venkat Kumar S, Tambuwala MM, Bakshi HA, Mehta M, et al. Antibacterial and antioxidant potential of biosynthesized copper nanoparticles mediated through Cissus arnotiana plant extract [Internet]. Vol. 197, Journal of Photochemistry and Photobiology B: Biology. 2019. p. 111531. Available from: http://dx.doi.org/10.1016/j.jphotobiol.2019.111531

[33] Ravindiran M, Praveenkumar C. Status review and the future prospects of CZTS based solar cell – A novel approach on the device structure and material modeling for CZTS based photovoltaic device. Renewable Sustainable Energy Rev. 2018 Oct;94:317–29.

[34] Ramamoorthi S, Nivedhitha MS, Divyanand MJ. Comparative evaluation of postoperative pain after using endodontic needle and EndoActivator during root canal irrigation: A randomised controlled trial. Aust Endod J. 2015 Aug;41(2):78–87.

[35] Malli Sureshbabu N, Selvarasu K, V JK, Nandakumar M, Selvam D. Concentrated Growth Factors as an Ingenious Biomaterial in Regeneration of Bony Defects after Periapical Surgery: A Report of Two Cases. Case Rep Dent. 2019 Jan 22;2019:7046203.

[36] Manivannan I, Ranganathan S,

Gopalakannan S, Suresh S, Nagakarthigan K, Jubendradass R. Tribological and surface behavior of silicon carbide reinforced aluminum matrix nanocomposite. Surf Interfaces. 2017 Sep;8:127–36.

[37] Sahay M, Sahay R. Rickets-vitamin D deficiency and dependency [Internet]. Vol. 16, Indian Journal of Endocrinology and Metabolism. 2012. p. 164. Available from: http://dx.doi.org/10.4103/2230-8210.93732

[38] Disabilities Of School Age Resulting From Rickets [Internet]. Vol. 201, The Lancet. 1923. P. 554–5. Available From: http://dx.doi.org/10.1016/s0140-6736(00)95427-8

[39] Anderson JJB. VITAMIN D | Rickets and Osteomalacia [Internet]. Encyclopedia of Human Nutrition. 2005. p. 378–82. Available from: http://dx.doi.org/10.1016/b0-12-226694-3/00056-9

[40] Holick MF. Osteomalacia and rickets [Internet]. Rheumatology. 2011. p. 1997–2005.e1. Available from: http://dx.doi.org/10.1016/b978-0-323-06551-1.00199-8

[41] Bartl R, Bartl C. Osteomalacia and Rickets [Internet]. Bone Disorders. 2017. p. 329–34. Available from: http://dx.doi.org/10.1007/978-3-319-29182-6_57

[42] Delgado J. Rickets and Osteomalacia Review [Internet]. Essential Orthopedic Review. 2018. p. 347–8. Available from: http://dx.doi.org/10.1007/978-3-319-78387-1_154

[43] Vijayashree Priyadharsini J. In silico validation of the non-antibiotic drugs acetaminophen and ibuprofen as antibacterial agents against red complex pathogens. J Periodontol. 2019 Dec;90(12):1441–8.

[44] Ezhilarasan D, Apoorva VS, Ashok Vardhan N. Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells. J Oral Pathol Med. 2019 Feb;48(2):115–21.

[45] Ramesh A, Varghese S, Jayakumar ND, Malaiappan S. Comparative estimation of sulfiredoxin levels between chronic periodontitis and healthy patients - A case-control study. J Periodontol. 2018 Oct;89(10):1241–8.

[46] Mathew MG, Samuel SR, Soni AJ, Roopa KB. Evaluation of adhesion of Streptococcus mutans, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary …. Clin Oral Investig [Internet]. 2020; Available from: https://link.springer.com/article/10.1007/s00784-020-03204-9

[47] Sridharan G, Ramani P, Patankar S, Vijayaraghavan R. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Oral Pathol Med. 2019 Apr;48(4):299–306.

[48] Pc J, Marimuthu T, Devadoss P. Prevalence and measurement of anterior loop of the mandibular canal using CBCT: A cross sectional study. Clin Implant Dent Relat Res [Internet]. 2018; Available from: https://europepmc.org/article/med/29624863

[49] Ramadurai N, Gurunathan D, Samuel AV, Subramanian E, Rodrigues SJL. Effectiveness of 2% Articaine as an anesthetic agent in children: randomized controlled trial. Clin Oral Investig. 2019 Sep;23(9):3543–50.