

## The Ancient Ossification-Diffuse Idiopathic Skeletal Hyperostosis

Anubha Bajaj\*

Department of Histopathology, Panjab University/A.B. Diagnostics, India

\*Corresponding Author: Anubha Bajaj, Department of Histopathology, Panjab University/A.B. Diagnostics, India.

Received: January 17, 2020; Published: February 18, 2020

### Preface

Diffuse idiopathic skeletal hyperostosis (DISH) is designated as a systemic condition with typical ossifying configurations which eventuate within the spine and peripheral entheses. Diffuse idiopathic skeletal hyperostosis was initially described by Forestier and Rotes-Querol in 1950 as a "senile ankylosing hyperostosis". The frequently applied nomenclature of diffuse idiopathic skeletal hyperostosis was denominated in 1975 by Resnick, *et al.* The characteristic ossification of spine canal and peripheral entheses, as cogitated in the systemic, diffuse idiopathic skeletal hyperostosis, can depict anterior ossification of thoracic spinal segments with consequent dysphagia and airway obstruction [1,2].

### Disease characteristics

Diffuse idiopathic skeletal hyperostosis frequently implicates the spine with appearance of pain and joint stiffness in the lumbar region.

Aforesaid spinal ossifications are characteristically delineated as "flowing" ossifications and classically necessitate the emergence of ossification at anterolateral segment of minimally three successive vertebral intersections or four contiguous vertebrae.

The infrequently delineated peripheral enthesopathy can arise within the shoulder, knee, elbow or calcaneus [3,4].

Diffuse idiopathic skeletal hyperostosis commonly appears on the rightmost portion of thoracic spinal segment. Significant ventral displacement of trachea and oesophagus is elucidated in diffuse hyperostosis which exemplifies dysphagia and airway obstruction. Diffuse hyperostosis additionally configures neo-bone anteriorly rather than laterally, concordant to the vertebral bodies. Approximately symmetrical distribution of ossification occurs in diffuse hyperostosis of the cervical spine. Displacement betwixt the vertebral bodies and trachea or oesophagus is significantly enhanced in diffuse hyperostosis [3,4].

Recent bone articulation in diffuse hyperostosis of the cervical spine is preponderantly anterior to vertebral bodies, in contrast to new bone deposition occurring antero-laterally in thoracic vertebral bodies. Diffuse hyperostosis of the cervical spine is symmetrical and concurrent to the sagittal midline, contrary to asymmetrical neo-ossification occurring within the thoracic spine.

Of obscure aetiology, diffuse idiopathic skeletal hyperostosis demonstrates a probable emergence in concomitant conditions of increased prevalence such as hyper-lipidemia, diabetes mellitus and hyper-uricaemia. Exemplification of immune antigens such as HLA-B8 is common in diffuse hyperostosis and diabetes mellitus. Diffuse hyperostosis lacks concurrence with antigens such as HLA-B27, in contrast to associated seronegative spondylo-arthropathies.

Diffuse idiopathic skeletal hyperostosis commonly appears in subjects beyond > 50 years and depicts an incidence of 25% in males and 15% in females with a comprehensive incidence of 6% to 12%. However, the prevalence is incremental beyond > 80 years with exemplification in 28% males and 26% females. Diffuse idiopathic skeletal hyperostosis enunciates an estimated detection of 22.7% in males and 12.1% in females, contingent to radiographic assessment of thoracic cavity.

The disorder commences at third to fifth decade and the clinical manifestations appear subsequently [3,4].

Diffuse idiopathic skeletal hyperostosis is frequently cogitated in Caucasians, in contrast to Blacks, Asians or Native Americans. Enhanced prevalence of diffuse hyperostosis is concurrent with attributes such as an elderly population, cardiovascular disorders and co-existing metabolic derangements.

Enunciation of a minimal bone density in diffuse idiopathic skeletal hyperostosis is debatable, although probability of vertebral fractures is enhanced with minimal trauma.

Diffuse idiopathic skeletal hyperostosis with spinal fractures demonstrate an increased incidence of ligamentous calcification and augmentation of deforming stress secondary to vertebral ankyloses.

### Disease pathogenesis

Diffuse idiopathic skeletal hyperostosis depicts a preponderant association with metabolic disorders such as diabetes mellitus, hyperuricaemia, obesity, dyslipidemia and hype-insulinaemia. Prospective mechanisms of emergence of characteristically articulated ossification in diffuse hyperostosis remains ambiguous. Factors incriminated in the pathogenesis of diffuse hyperostosis are superimposed mechanical stress and strain to implicated bones and joints, exposure to diverse toxins and a distinct genetic predisposition. Angiogenesis is a common factor in the enunciation of clinical features of diffuse hyperostosis.

Metabolic syndrome demonstrates an enhanced incidence of carotid atherosclerosis and diffuse hyperostosis. Prevalence of aortic valve sclerosis in diffuse idiopathic skeletal hyperostosis appears concomitant to the emergence cardiovascular events [4,5].

Vascular configurations function as natural barriers in neo-ossification and recently articulated bone in diffuse hyperostosis, as thoracic ossification predominantly occurs contralateral to thoracic aorta. Thoracic ossifications are attenuated in zones with a horizontal enunciation of segmental arteries, abutting the vertebral bodies. Spinal ossification is indented with arterial branching, thereby indicating the mechanical impediment of pulsating vasculature upon the soft tissue ossification. Aforesaid manifestation exemplify the typical undulating, "flowing" arrangements of ossification.

Cervical spine demonstrates notable vertebral arteries such as common carotid, internal carotid and external carotid arteries which are symmetrically situated lateral to vertebral bodies. Prominent segmental arteries of significant calibre may not horizontally traverse the vertebral bodies [4,5].

Enlarged vasculature prevents the configuration of neo- bone in diffuse hyperostosis. Recently arranged bone within the cervical spine is situated in the midline and expands ventrally, with eventual displacement of oesophagus and trachea.

Vertebral and carotid arteries are commonly situated lateral to vertebral bodies of cervical spine. Segmental vessels remain devoid of planar radiographic detection.

Subacute onset of clinical symptoms signifies the emergence a mechanical obstruction with gradual evolution of neo-bone, a feature which is predominant in the pathogenesis of diffuse hyperostosis.

Anterior location of recent ossification can ensue secondary to inducing factors such as repetitive elongation of degenerated anterior longitudinal ligament with subsequently appearing ossification [3,5].

### Clinical elucidation

Diffuse idiopathic skeletal hyperostosis of the spine commonly arises within the right thoracic region. Mechanical barricade to the emergence of diffuse hyperostosis on contralateral positions is provided by a pulsatile, descending thoracic aorta.

Articulations of ossification in cervical and lumbar zones within diffuse hyperostosis are manifested diversely. However cervical and

lumbar regions depict a symmetrical, non marginal syndesmophyte ossification in diffuse idiopathic skeletal hyperostosis.

Typical manifestations of diffuse idiopathic skeletal hyperostosis frequently emerge in the anterolateral portion of the thoracic spine, contralateral to descending thoracic aorta. Aforesaid modifications exhibit a classical bridging ossification, recapitulating a “flowing candle wax” appearance on the lateral view of obtained plain radiographs [6,7].

Traditionally, three specific diagnostic criterion define diffuse idiopathic skeletal hyperostosis:

- i) Appearance of vertebral “flowing ossifications” at a minimum of four contiguous vertebrae.
- ii) Maintenance of intervertebral disc height and an absence of preponderant degenerative modifications within the integrated vertebral segments, features which adequately demarcate diffuse idiopathic skeletal hyperostosis from degenerative spondylosis.
- iii) Absence of ankyloses is concurrent at the facet- joint interface along with the absence of erosion, sclerosis or fusion of sacroiliac joint, features which segregate diffuse idiopathic skeletal hyperostosis from ankylosing spondylitis.

Contemporary definition of diffuse idiopathic skeletal hyperostosis necessitates a modification as it is applicable to significantly advanced disease stages. It has been recommended to reduce the spinal incrimination to two contiguous vertebrae in addition to inclusion of peripheral enthesopathies [2-4].

Following elements also require inclusion:

- i) Occurrence of exuberant new bone formation in the vertebrae, sacro-iliac joint and facet-joint interface at adjunctive locations.
- ii) Bridging of expansive, bony articulations within the cervical, thoracic or lumbar spine.

Diffuse idiopathic skeletal hyperostosis demonstrates minimal clinical symptoms in contrast to extensive modifications detected on radiography or methodologies of advanced imaging. Diffuse idiopathic skeletal hyperostosis can be discovered incidentally in subjects who are essentially asymptomatic.

Classical clinical representation is denominated by an elderly individual displaying lumbar pain or back stiffness of increasing intensity. Ossification and bone deposition within the cervical spine is generally asymptomatic. However, clinical symptoms such as dysphagia with consumption of solids, fluid aspiration, hoarseness, regurgitation, sleep apnoea, upper respiratory tract infection, airway obstruction and arduous endotracheal intubation is delineated on account of incriminated soft tissues depicting abutting, secondary bony osteophytes within the cervical vertebral segments [6,7].

Elderly subjects with acute on chronic lumbar pain and co-existent minor trauma can raise the possibility of diffuse hyperostosis. Contiguity of osseous fusion within the spinal vertebrae enhances the predisposition to fractures.

Incrimination of peripheral joints with diffuse hyperostosis is specific and describes:

- i) implication of joints commonly uninvolved by primary osteoarthritis such as hip or knee.
- ii) Foot and ankle joints are delineated in an estimated 70% individuals.
- iii) Clinical and radiographic features are indicative of heel spurs, Achilles tendinitis and plantar fasciitis.

- iv) Hypertrophic manifestations within the implicated joints are enhanced, in contrast to primary osteoarthritis.
- v) Enthesopathies are predominant, particularly adjacent to peripheral joints.
- vi) Enthesis undergo distinct calcification and ossification, especially in sites disparate from peripheral joints [6,7].

Investigation of peripheral joints depict hyperostosis and tendonitis. Pelvic region can demonstrate enthesophytes within the iliac wing and ischial tuberosity. Periarticular hyperostosis and ossifications of the tendon arise in the hip, knee, shoulder, hand, elbow and wrist.

### Histological elucidation

Morphology of neo-formative bone appearing within the cervical spine is diverse from thoracic spine on account of the dissimilar, localized vascular morphology. Superficial surface of recently configured bone is symmetrically situated anterior to the vertebral bodies.

Concordant inflammation of soft tissues can contribute to dysphagia and airway obstruction. Inflammation can envelop the ossification with consequent nerve entrapment and restricted mobility of the epiglottis, larynx along with retention of solid food [3,4].

### Differential diagnosis

Distinction of diffuse hyperostosis from ankylosing spondylosis is crucial. Criterion advocating the emergence of diffuse idiopathic skeletal hyperostosis include an advanced age of disease presentation, lack of obliterated apophyseal joints, frequent ossification of the anterior longitudinal ligament (ALL), absence of peripheral enthesopathies with bony erosions, appearance of a milder or painless disease and absence of incrimination of sacro iliac joint.

It is imperative to discern the milder variants with clinical symptoms of incriminated sacro-iliac joints, particularly the appearance of sacro-iliac osteophytes in diffuse hyperostosis [8,9].

Subjects with lumbar pain, joint stiffness and spondylophytosis necessitate a segregation from:

- Ankylosing spondylitis
- Spondylosis deformans, a condition which lacks the ossification of thoracic anterior longitudinal ligament (ALL).
- Seronegative spondyloarthropathies
- Charcot's spine
- Acromegaly
- Psoriasis
- Reiter's syndrome
- Pseudo-gout
- Hypoparathyroidism [3,4].

### Investigative assay

Comprehensive neurovascular examination is mandated along with radiographic or advanced imaging of entire spinal column in order to prevent a possible omission of fractures in adjacent vertebrae. Classically, an asymmetrical "flowing" ossification is delineated in the thoracic spine or incriminated locations.

Categorical criterion for establishing a diagnosis of diffuse idiopathic skeletal hyperostosis as defined by Resnick et al incorporate a minimal vertebral ossification span of four contiguous vertebrae and an absence of grossly visible degenerative modifications within the intervertebral disc or sacro-iliac and apophyseal joints [3,4].

Typical serological parameters such as erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), rheumatoid factor (RF) and anti-nuclear antibody (ANA) are within range in diffuse hyperostosis.

Radiographic examination with antero-posterior and lateral spine imaging in diffuse hyperostosis demonstrates a “flowing candle wax” appearance with the occurrence of non-marginal syndesmophytes with horizontal vertebral projection and a configuration of extra-articular ankyloses. Aforesaid manifestations are distinct from the vertical “bamboo spine” which articulates the ossification of intra-articular disc space in ankylosing spondylitis. Enhanced radio-density, preservation of facet joints and intervertebral disc space, as elucidated on imaging of the vertebral column, can aid the distinction of diffuse hyperostosis from ankylosing spondylitis, a condition which depicts osteopenia and degenerative alterations [8,9].

Moribund subjects with osteoporosis can depict compression fractures of the vertebra. Thus, preliminary radiographic assessment of thoracic spine or chest cage is necessitated in primary cervical or lumbar pain, joint stiffness or diffuse involvement of extremities.

Discernment of diffuse hyperostosis is contingent to adequate and competent imaging of the thoracic spine, a manoeuver which can prevent additional assessment or a surgical intervention.

Sagittal view of cervical spine on plain radiographs or computerized tomography can depict “non-flowing” ossifications and can be devoid of discernible segmental vessels.

Assessment of cervical and sacroiliac joints is mandated. Distinction from conditions such as ankylosing spondylitis or spondylosis with fused facet joints is necessitated. Normal anatomical location of cervical vasculature recently arranged bone, trachea and oesophagus requires elucidation [9,10].

Assessment of vertebral bodies at cervical levels C4, C5, C6 are mandated as the hyperostosis is maximally enunciated as aforesaid levels. Radiographs at mid-sagittal and anterior- posterior planes can decisively delineate the location of neo- bone as it appears anterior and lateral to the implicated vertebral body. Symmetry, magnitude and degree of configured new bone requires evaluation along with proportionate displacement of trachea and oesophagus [3,4].

Application of technetium bone scan in diffuse hyperostosis can demonstrate an enhanced radioactive uptake within the incriminated regions. Radioactive uptake is inadequate in non-traumatic instances. Diffuse hyperostosis requires a segregation from metastatic tumour.

Implication of lumbar spine can be evaluated by plain radiographs of lumbar region and pelvis, as instances of sacroiliac joint involvement can misrepresent the occurrence of associated conditions, particularly seronegative spondyloarthropathies [3,4].

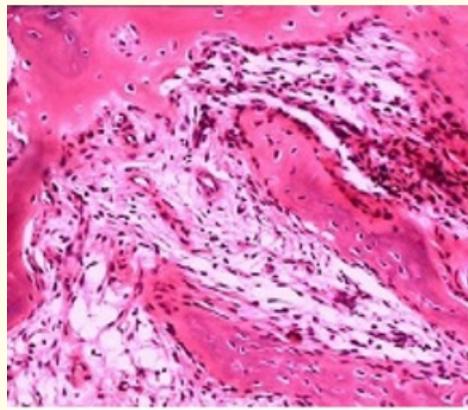
Minimal degrees of trauma in diffuse idiopathic skeletal hyperostosis can induce fracture and joint instability. Sequestered or undetected injuries can initiate a neurological malfunction and delayed therapeutic intervention. Occult fractures require an aggressive evaluation with advanced imaging techniques such as computerized tomography (CT), magnetic resonance imaging (MRI) or computerized (CT) myelogram. Contemporary ossification and bony articulation of the cervical spine can be adequately examined by computerized tomography in subjects of symptomatic diffuse hyperostosis and spatial configuration of neo-bone can be concurred with arterial vasculature, trachea and oesophagus. Extra-spinal symptoms of diffuse idiopathic skeletal hyperostosis can be appropriately evaluated with simple radiographs [9,10].

### Therapeutic options

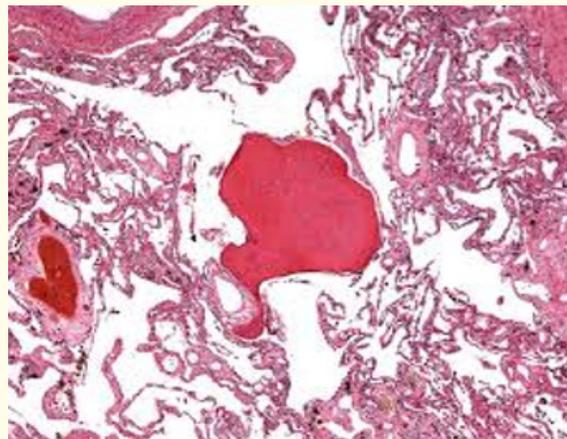
Symptoms such as singular lumbar discomfort can be managed with modification of degree of activity, physical therapy, employment of spinal braces, agents such as non-steroidal anti-inflammatory drugs (NSAIDS) and bisphosphonates. Surgical decompression and spinal stabilization is preferred in specific sequelae such as vertebral fractures, cervical myelopathy, lumbar stenosis, neurological dysfunction, secondary infection or delineation of painful deformities.

Surgical intervention of elderly population with cervical fractures concomitant to diffuse idiopathic skeletal hyperostosis depicts a 15% proportionate mortality, in contrast to an estimated 67% following the employment of conservative therapy. Thus, a prompt diagnosis, evaluation and appropriate treatment sequential to a traumatic episode is mandated in diffuse idiopathic skeletal hyperostosis [3,4].

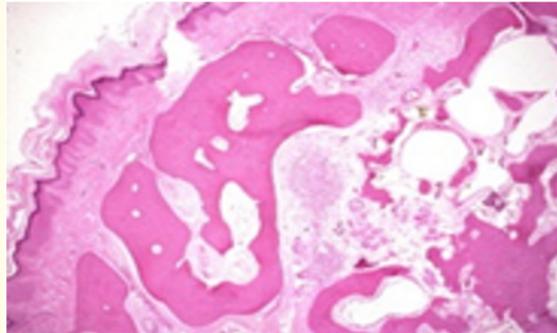
Heterotopic ossification is a frequent complication, encountered in an estimated 30% to 56% subjects of diffuse hyperostosis undergoing total hip arthroplasty. However, a therapeutic prophylaxis is not recommended in instances of heterotopic ossification occurring in diffuse hyperostosis following total hip arthroplasty [8,10].



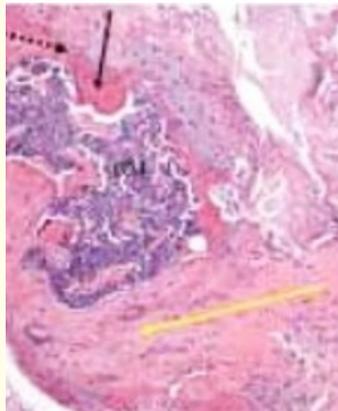
**Figure 1:** Fibrous tissue, trabecular bone and spindle cells entrapped in connective tissue in diffuse idiopathic skeletal hyperostosis [11].



**Figure 2:** Diffuse idiopathic skeletal hyperostosis with new bone formation and circumscribing connective tissue [12].



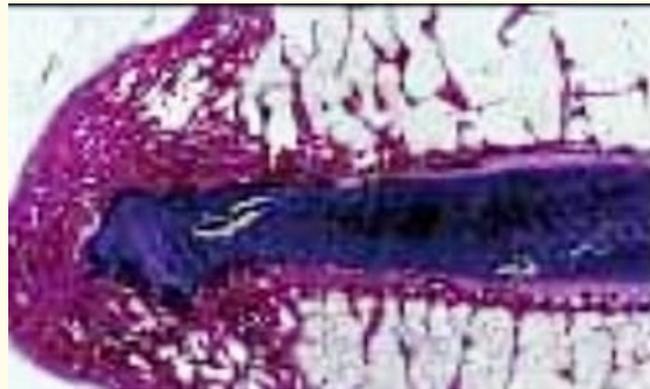
**Figure 3:** Diffuse idiopathic skeletal hyperostosis with trabeculae of neo-formed bone and enveloping fibrous tissue with a superimposition of hyperkeratotic, stratified squamous epithelium [12].



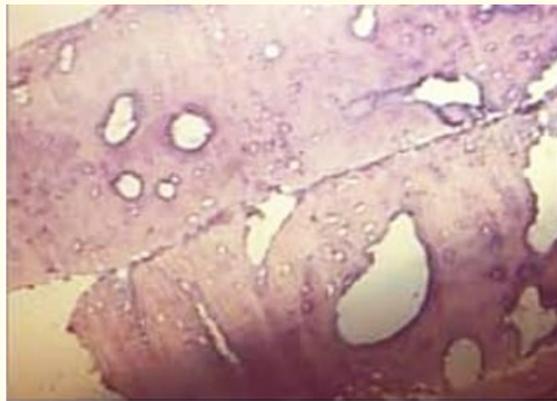
**Figure 4:** Diffuse idiopathic skeletal hyperostosis with curvilinear bony trabaculea and un-inflamed encompassing fibro-connective tissue [13].



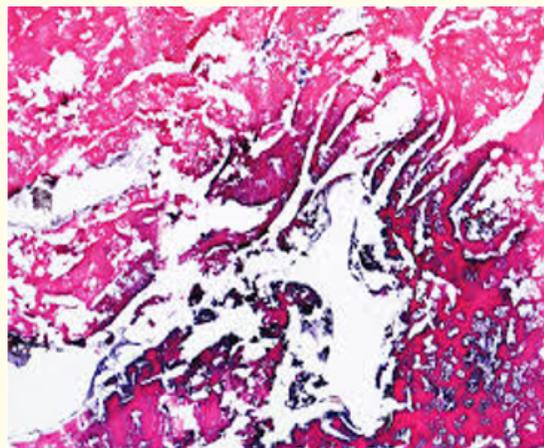
**Figure 5:** Diffuse idiopathic skeletal hyperostosis with dense bony fragments and enveloping fibro-connective tissue [14].



**Figure 6:** Diffuse idiopathic skeletal hyperostosis with elongated, trabecular bone and a thinned out, surrounding connective tissue [14].



**Figure 7:** Diffuse idiopathic skeletal hyperostosis with bony trabeculae, haversian canals and a circumscription of fibrous soft tissue [15].



**Figure 8:** Diffuse idiopathic skeletal hyperostosis with fragments of bone and dense, uninfamed fibro-connective tissue [16].

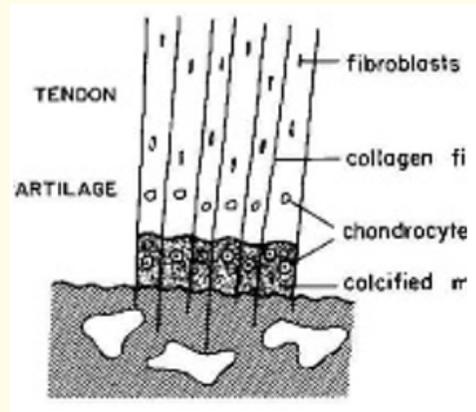


Figure 9: Graphic delineation of peripheral enthesis in diffuse idiopathic skeletal hyperostosis [17].

### Bibliography

1. Forestier J and Rotes-Querol J. "Senile ankylosing hyperostosis of the spine". *Annals of the Rheumatic Diseases* 9.4 (1950): 321-330.
2. Resnick D., et al. "Diffuse idiopathic skeletal hyperostosis- Forestier's disease with extra-spinal manifestations". *Radiology* 115.3 (1975): 513-524.
3. Luo DT and Varacallo M. "Diffuse idiopathic skeletal hyperostosis". Stat Pearls Treasure Island (FL) (2019).
4. Bakker JT, et al. "Morphological characteristics of diffuse idiopathic skeletal hyperostosis in the cervical spine". *Plos One* 12.11 (2017): e0188414.
5. Maden R., et al. "Diffuse idiopathic skeletal hyperostosis- clinical features and pathogenic mechanisms". *Nature Reviews Rheumatology* 9.12 (2013): 741-750.
6. Mader R., et al. "Serum adiponectin levels in patients with diffuse idiopathic skeletal hyperostosis (DISH)". *Clinical Rheumatology* 37.10 (2018): 2839-2845.
7. Pariente-Rodrigo E., et al. "Relationship between diffuse idiopathic skeletal hyperostosis, abdominal aortic calcification and associated metabolic disorders: data from Camargo Cohort". *Medicina Clínica* 149.5 (2017): 196-202.
8. Orden AO., et al. "Association of diffuse idiopathic skeletal hyperostosis with aortic valve sclerosis". *Medicina (Buenos Aires)* 74.3 (2014): 205-209.
9. Hirasawa A., et al. "The prevalence of diffuse idiopathic skeletal hyperostosis in Japan- the first report of measurement by CT and review of the literature". *Journal of Orthopaedic Science* 21.3 (2016): 287-290.
10. Sohn S., et al. "Increased bone mineral density in cervical or thoracic diffuse idiopathic skeletal hyperostosis: a case control study". *Journal of Clinical Densitometry* 21.1 (2018): 68-74.

11. Image 1 Courtesy: Dove Medical Press.
12. Image 2 and 3 Courtesy: Science direct.
13. Image 4 Courtesy: T space, University of Toronto.
14. Image 5 and 6 Courtesy: Wiley online library.
15. Image 7 Courtesy: *International Journal of Anatomical Science*.
16. Image 8 Courtesy: Two sci.u.szeged.hu.
17. Image 9 Courtesy: Semantic Scholar.

**Volume 3 Issue 3 March 2020**

**©All rights reserved by Anubha Bajaj.**