OSTEOPOROSIS AND *ASTHIKSHAYA*

-PATHOPHYSIOLOGY AND PRINCIPLES OF MANAGEMENT.

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Osteoporosis is an important ailment commonly overlooked by clinicians. Being usually asymptomatic, it is also called as a "silent killer disease". Patients are usually unaware of their disease until fracture occurs. Patient lands up in a hospital after an unexpected fracture.

It is estimated that in 2003, 2.5crore women in India had osteoporosis. This number is expected to rise by further one Crore in next decade. More than 20 Crore women all over world have osteoporosis. Over 15% females over 50 years age in United States have osteoporosis, whereas additional 35-50% are supposed to have osteopenia at hip.

Average age of population is on rise. Average age of Indian population is 62years at present (47 years in 1947). Decadal growth rate for population above 60 year age is 5-8% higher than that for total population. India is expected to have 11 Crore senior citizens (> 60 year age) by year 2015. Aging, too, is an important cause of osteoporosis.

Osteoporosis is an important cause of fractures especially at wrist, hip and vertebra. The cost of inpatient and community care of these fractures was estimated in 1995 at 7 billion and $ 14billion in UK and USA respectively. Considering the gravity of this problem, World Health Organization set up an expert advisory group in 1994 to study gravity of situation and definition of this disease in general. The current classification and research in osteoporosis are based on these WHO recommendations.

DEFINITION

WHO defines osteoporosis on the basis of bone density. Low bone mass is an important feature. Total and regional as well as mineral and osteoid bone mass are reduced. There is micro architectural deterioration of bone tissue leading to increased bone fragility. Fragility means compromised bone strength which reflects integration of two main features, bone density and bone quality. Increased bone fragility leads to increase in fracture risk.

Kshaya means loss , decline, decay, diminution or waning. Dalhan has aptly defined *kshaya* as '*swapramanhaani*' (S. Su. 15/24) whereas Chakrapanidatta describes it as rahasaha. or *nyuntvam* (Ch. Su. 17/4). These three Sanskrit words together are more than sufficient to explain the present concept of *asthikshaya*.

Various terms such as *asthisaushirya, asthidaurbalya, asthishieeran , ashitlaghav, asthishunyata, riktata* and *asthimardav* appear in Ayurveda texts to describe *asthkshaya.*

WHO defines low bone mass on the basis of T score i.e. standard deviation (SD) of bone mineral density (BMD) with reference to mean of young adult population.
T Score:

0.00 to −1.00	Normal
-1.00 to -2.5	Osteopenia
< -2.5	Osteoporosis

WHO defines low bone mass on the basis of T score i.e. standard deviation (SD) T score of less than -2.5 SD and evidence of one or more fragility fractures means established osteoporosis. A fragility fracture is one which occurs due to fall from no greater than standing height of an individual or with normal use. The present epidemiological data on osteoporosis is based on these definitions.

PHYSIOLOGY OF BONE

Bone is a live tissue. It has blood vessels and nerves. Skeleton is highly vascular- it receives 10% of cardiac output. Bone grows, heals when fractured and remodels if fracture is misaligned. Unnecessary bones get reabsorbed.

Bone has 2 components:
1) Fibrous tissue which gives resilience and toughness and
2) Mineral which gives hardness and rigidity.

Collagen fibers have tensile strength like tendons. Mineral salt have compressional strength. Minerals i.e. calcium, phosphorus, zinc, magnesium, fluoride, etc are in the form of needle shaped crystals of hydroxyapatite and are arranged around collagen fibers. 35% of dry bone is osteoid i.e. organic ground substance (matrix made up of glycoprotein and collagen fibers Type 1). Bone has following types of cells:
1) Osteoprogenitor cells i.e. stem cells of mesenchymal origin converted to osteoblast when required.
2) Osteoblasts- Bone forming cells which lay down organic matrix and collagen fibers around which crystals are deposited.
3) Osteocytes provide nutrition to bone.
4) Osteoclasts- Large multinucleated bone removing cells derived from monocytes secretes acid and proteolytic enzymes that degrade bone.
Bone is a dynamic structure. The calcium ions are not fixed and are constantly interchanged with calcium in circulation. 18% of total skeletal calcium is replaced each year (just are RBCs are replaced every 120days- *chakravat parivruttihi*). Bone remodeling begins with resorption of bone by osteoclasts forming a "pit" which is subsequently mineralized by osteoblasts. Remodeling removes weak and

older bone which is replaced by strong new bone in skeletal areas subjected to mechanical stress.

Some important references in Ayurveda need to be cited here.

1) *Upadhatu* do not have *gati*. *Gati* is an important feature of all *dhatus* including *asthidhatu*[1] (Chakrapani C. Chi. 15/15)

2) *Asthi* is accepted in a liquid form (Chakrapani C.Vi.5/8) [2]. This liquid *asthi* is present in minute quantities (?ionic free calcium) and hence not quantified as *anjalipraman* of body fluids (C. Sha. 7/15).

3) Sushrut has not described *asthivahartrotas* in *viddhalakshan* as it extends throughout body (Dalhana S. Sha. 9/12)[3].

4) The entire body including bones is *chetan* except nails and hair (Chakrapani C. Vi. 5/7)[4].

5) *Asthiposhan* is a function of *medodhatu* (S. Su. 15/5)[5].

6) *Asthidhatwagni* has peculiar action. The *sanghat* is made *khar* i.e. hard, solid, dense or thick (i.e. mineralization only) by *asthidhatvagni* (C. Chi. 15/31)[6]. It is important to note that mineralization cannot occur without osteoid (cells and fibers)

7) The porosity of bone is due to *Vayu* and *Aakash* amongst other factors (C. Chi. 15/33).

FACTORS IN BONE HEALTH

1) Calcium- Adequate dietary calcium (400mg per day) is essential. Increased gastric acidity, high protein diet, lactose in milk favor absorption. Milk is best source of calcium. Shrimp, crab and vegetables like spinach *(palak)*, colacasia *(aalu)*, gingili seeds *(teel)*, agathi *(agasthi)*, drum-stick leaves *(shigrupatra)* and amaranth *(math)* are also good sources. Oxalic acid in vegetables and phytates in cereals inhibit calcium absorption. High salt intake, lack of exercise, smoking, caffeine, alcohol, carbonated beverages and drugs like steroids, thyroxin and anticoagulants have negative impact on calcium balance. Increased gastrointestinal motility as in *grahani*, laxative abuse and steatorrhoea (fatty acid + calcium=soap) impair calcium absorption. Calcium is excreted in urine. Inadequate reabsorption in chronic renal failure increases calcium losses.

2) Exercise- Weight bearing exercise is essential for bone health. Stress and strain makes bones denser. Bedridden people loose up to 5% bone each month. Even rest in pregnancy causes demineralization. Swimmers and astronauts suffer calcium loss. It would be interesting to note that advantages of exercise are similar to a *asthisarata* (C. Su. 7/32[8], C. Vi. 8/109[9]).

3) Vitamin D- Vitamin D, considered to be hormone itself, is essential for calcium homeostasis. It facilitates calcium absorption from gut and resorption from renal tubules. This fat soluble vitamin is synthesized under skin by photo biogenesis in presence of ultraviolet rays in sunlight. This vitamin D3 is further transformed in liver and kidneys to dihydroxy D3, the physiologically active hormone form. Adequate sunlight is thus necessary for bone health.

Pardah, ghunghat, dark skin are detrimental to bone health. Milk drawn towards evening has special properties (S. Su. 45/60).

4) <u>Parathyroid hormone</u>- This maintains plasma calcium levels by calcium mobilization from bones. Plasma calcium level is more important as this free ionized calcium is essential for various actions like blood clotting, neuromuscular transmission, muscle contraction and relaxation, etc.

5) <u>Sex hormones</u>- Both androgens and estrogen promote mineral deposition and bone growth by increasing osteoblastic activity. They are responsible for bone maturation and make bone matrix thicker.

6) <u>Peak Bone Mass</u> is achieved at the age of 30 years in males and somewhat earlier in females. Both sexes loose 0.7% to 1% of bone mass for the rest of their life. Age related bone loss is more marked in females. They can loose over 2% of bone mass each year during initial 5-6 postmenopausal years. Growth stops at age of 20 and waning starts at age of 30 (Sha. S. I/6/20)[11]. It is therefore important to invest in bone health before this age with appropriate diet and exercise. *Rasayanchikitsa,* too, needs to be carried out upto *madhyavay* (S. Chi. 27/3)[12]- middle age (*youvan* upto 30years, *madhyavay* upto 60years)

AETIOLOGY AND CLASSIFICATION

Osteoporosis is of 3types. Type1 is post menopausal and can occur from 2-3 years before to 15-20years after cessation of menses. Lack of estrogen is primary factor leading to uninhibited osteoclastic activity. Type2 is senile osteoporosis occurring in men and women with equal frequency. This osteoporosis is caused by inability of kidney to produce active vitamin D as well as by decrease in osteoblastic activity. Both these types are classified as idiopathic, with no identifiable cause. They are also classified as high turnover (increased bone resorption by osteoclasts) and low turnover (decreased osteoblastic activity) osteoporosis respectively.

Type3 osteoporosis is secondary to other causes such as hyperthyroidism, hyperparathyroidism, inflammatory bowel disease, malabsorption syndromes, chronic renal failure, drugs, etc.

Asthi-asaar is an important feature of senility. This is also called as *apratyagra dhatutva (jirna)* by Sushruta requiring more time for fracture healing in elderly individuals (A. S. Sha.8/24)[13].

Menopause, too, is considered to be a feature of senility by Ayurveda (S. Sha. 3/11)[14]. Menstruation is also proposed to be *strotah shodhan* by some of the commentators. Lack of menstruation causes *strotorodh* (S. Chi. 13/33)[15]and impairs *anulom gati* of *Vaatdosha*, leading to its *prakop* i.e. high bone turnover osteoporosis.

PATHOLOGY

Loss of bone mass is hallmark of osteoporosis. The bony trabeculae are thinner and are more widely separated than usual, resulting in increased susceptibility to fractures. There is no alteration in the ratio of minerals to protein matrix i.e. the mineral content of remaining bone is normal. *Saushirya* is an action of *vaatdosh* (C. Chi. 15/31)[16]. *Asthishosh* and fractures are a feature of *asthigatvaat* (S. Ni. 1/28)[17]. *Medodhatu* provides nutrition to *asthidhatu (asthipushti)* whereas *asthisoushirya (douvarbalya, laghav)* is a feature of *majjakshaya*. This *snehaparampara* needs to be born in mind during study of *asthikshaya*.
Sushrut has described 7 types of *Shoshavyadhi*. *Shosha* by itself is a *vaatprakop lakshan* (V. Su. 12/50). *Kshay, Rajyakshama,* etc are the alternative terms for *Shosh*. One of the types, *sthaviryashosh* is due to *asthikshay*. This means that various features of senile degeneration are due to *asthidhatu kshaya*. Nutrition of all *dhatu* is dependent upon diet (S. Su. 14/11)[18]. It seems that even a proper diet is unable to nourish *dhatu* which are aging (S. Su. 14/19[19],S. U. 41/4,27[20]) Madhavnidan describes *Rajayakshma* as *anulom* and *pratilom* (M.Ni. 10/2)[21].It can be seen that the *samprapti* of *Rajyakshma* encompasses Type1 and Type2 osteoporosis or high turnover and low turnover osteoporosis respectively.
It seems that modern medicine is concentrating more on mineral rather than osteoid in diagnosis and treatment of osteoporosis. Ayurveda gives more weightage to osteoid and treats osteoporosis with *snigdha* medications. This appears more appropriate in view of the fact that osteoid is formed first which is then followed by deposition of mineral in relation to fibers.

CLINICAL FEATURES

There are no specific clinical features of osteoporosis except back pain and propensity for fracture after trivial trauma. Wrist and hip fractures cause considerable morbidity. Hip fractures at this age have 15-25% mortality in one year and 70% of survivors have compromised function. Vertebral fractures, though usually painless, cause kyphosis (loss of height-widow's hump), disability, reduced quality of life and reduction in vital capacity of lungs.
As there are no specific features of osteoporosis, the subtle features of *Asthi khaya* (C. Su. 17/67, S.Su. 15/9, V. Su.11/19, Bhav Prakash p.323) along with those of *Asthigata Vata* (S. Ni. 1/28) and *Asthi asaratwa* (C. Vi. 8/112) described in Ayurveda need to be carefully looked for. These features are as follows:

Falling of hair (alopecia)	Dryness
Falling of lanugo hair (*Loma*)	Laxity of joints (*shaithilya*)
Loss and breaking of nails	Bone pains (*shool, toda*)
Loss of facial hair	Lack of vigor
Loss and breakage of teeth	Inactivity
Desire of meat containing *majja*, *asthi* and *sneha*	Inability to bear pain/over work (*klesh*)
Fractures	*Asar sharer*
Laghuta of heel, ankle, etc	*Asthir sharer* (tremulous)
Fatigue	

The features of fatigue, dryness, alopecia, nail and teeth disorders, laxity of joints and desire for particular food need to be studied in this context.

MODERN DIAGNOSTIC METHODS

1) <u>X ray</u>- Conventional radiographs are insensitive and unreliable as features are apparent only after 30-50% of bone loss.
2) <u>DEXA</u>- (Dual Energy X ray Absorptiometry) gives best accuracy and least radiation. The WHO classification of osteoporosis is based on DEXA measurements. Central or axial (spine and hip) DEXA measurements require larger machines but are best predictors of fracture risk. Peripheral DEXA (heel, radius) is more widely available and is least expensive. The T score compares bone mass of patient with that of young (30year) normal subject, whereas Z score is comparison with age matched subject. One SD below mean level implies about 12% loss of BMD and fracture risk doubles with each negative SD.
3) Other methods-like quantitative computed tomography (QCT) and quantitative ultrasound (QUS) can also be used but have limitations. Bone biopsy is used for research purposes only.
4) Bone markers are biochemical markers of bone turnover. They provide assessment of global disease activity throughout skeleton. Two types of markers are used-
a) Formation markers (osteoblastic activity).
   - Alkaline phosphatase
   - Osteocalcin (GLA protein)
   - Procollagen-1-N-peptide (P1NP)
b) Resorption markers (osteoclastic activity).
   - Acid phosphatase
   - C-telopeptide
   - Urinary-N-telopeptide

A combination of DEXA and bone biochemical markers along with biopsy in selected cases can give necessary objective data for assessing   efficacy of treatment in osteoporosis. These methods should be used for trials of Ayurvedic drugs in osteoporosis.

PRINCIPALS OF MANAGEMENT

The following points should be kept in mind while treating osteoporosis.

1) There is no single drug which can be *snigdha* as well as *shoshan*[22]. *Tiktarasa is shoshan and increases kharguna. Snigdhatva* is brought about by milk or ghee. *Guduchi* (Tinospora cordifolia), *Katuka* (Picrorhiza curroa), *Nimba* (Azadirachta indica), *Kutaja* (Holarhenna antidysenterica), *Ativisha* (Aconotum heterophyllum), *Brihat-panchamool* as also *kansya*, *loha, praval* (coral), *shankha* and *shukti* are important *tikta* medicines. These are aimed at treating the osteoid rather than mineral.

2) *Basti* is an important therapy in *asthikshaya* management[23]. *Asthidharakala* is same as *purishdharakala.* Hence large bowel is of particular importance in management of bone related disorders.

3) Recent studies in Japan indicate that submaximal heating (800 degree Celsius) of oyster shell and mixing it with similarly heated seaweed gives best absorbable calcium[24]. Calcium containing *bhasmas* in Ayurveda are similarly prepared. Ayurveda does not advocate them for *asthikshay*. They are known to be acid suppressants, which itself reduces calcium absorption. They are *grahi* and cause some constipation. Their effect on *pachakagni* in general and *asthidhatvagni* in particular needs further studies.

4) Phytoestrogens are plant derived molecules having estrogenic actions- increase osteoblastic activity, bone matrix formation and mineral deposition. They are present in many foodstuffs including beans, sprouts, cabbage, spinach, soybeans, grains as also asparagus, garlic, licorice, orange, etc. Many of our *tikta* and other plants also contain phytoestrogens. It would be interesting to know the percentage of phytoestrogens in these plants.

5) Role of milk, exercise and sunlight are already discussed. As peak bone mass at age of 30 is important, any form of *rasayan* should be used before this age. It must also be realized that *aahar ras* becomes *apreenan* (can not nourish) in elderly individuals.

6) High protein intake is advisable. Lower protein intake is significantly related to bone loss at fracture prone sites. Proteins are essential for development of osteoid. Use of *mansras* (meat soup) is, therefore, advisable.

7) Use of *swayonivardhan dravya* is, also advisable. *Tarunasthi* should be used in this context. *Ajasthibhsma* and *kurmaprushthabhasma* are particularly important.

8) Finally, *lavan,kshaar, amla, ruksha* and *katu* is not advisable *(apathya)* in fracture management. This principal also applies to management of osteoporosis as these two are interrelated.

9) *Asthidhatu* Is manufactured in later stages of metabolism. It must be realized that treatment of *asthikshaya* is of a prolonged nature and follow-up DEXA should be carried out at the end of one year only.