



Postmenopausal Osteoporosis Awareness & Management in Women-An Indian Perspective

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Review Article

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Abstract

Postmenopausal osteoporosis affects millions of women each year jeopardising their healthcare and quality of life. Initial treatment is based on many factors including T-score, fracture risk assessment tool score, and risk factors for fractures. The most recent additions to treatment are aimed at those who are considered to be at higher fracture risk. The newest FDA-approved medications, abaloparatide and Romosozumab that work to increase bone formation in 18 and 12 months, respectively. Due to lack of awareness in Indian women and with the increase in life expectancy as proved by recent studies, it's important to find out new medications and better lifestyle options for better management of Postmenopausal osteoporosis to help avoid fragility fractures and improve the quality of life of the Indian women.

Keywords: Menopause; Osteoporosis; Postmenopausal; Antiresorptive

Abbreviations: BTMs: Bone Turnover Markers; BMI: Body Mass Index; PTH: Parathyroid Hormone; HRT: Hormone Replacement Therapy; QUS: Quantitative Ultrasound; DXA: Dual Energy X-Ray Absorptiometry; MOF: Major Osteoporotic Fracture.

Background

Menopause is the time of cessation of the menstrual cycle in women. The development of ovaries decrease and a natural decline is observed in the sex hormones. This period may be related to an expansive assortment of indications influencing the urogenital and circulatory frameworks, as well as hair, bone and skin. The sum of Bone cells amassed by the conclusion of the moment decade and remains more or less consistent up to the time of menopause. The lack of sex hormones like estrogens, results in too quickened bone resorption and replacement, a negative adjust and micro-architectural weakening, which compromises with bone quality, as a result of that bone fragility increases, that leads to risk of fracture.

Currently, it is estimated that over 200 million people worldwide suffer from this disease [1]. By the age of 80, it is computed that half of trabecular bone will have been lost. Normal menopause happens between the ages of '45 and 54' years everywhere on the world. This age doesn't seem to have changed fundamentally throughout the long term. Interestingly, since the center of the nineteenth century, future, especially in ladies, has expanded impressively, with most ladies living to the age of 80 years or more in numerous locales of the world. This implies that at 50 years old years, a lady will live for over 30 years without bone assurance by sex hormones. This speaks to more than 33% of a lady's life. At 50 years old years, the lifetime danger to encounter a crack is about half (i.e., one out of two ladies will have a break during this period. In India, the prevalence of osteoporosis in postmenopausal women in various studies varies between 25% and 62% [2]. In 2008, it was assessed that in excess of 700 million ladies were more seasoned than 50 on the planet. This number should arrive at 1.2 billion by 2030.

Osteoporosis is the most common metabolic bone disease in humans. According to the 1993 International

consensus, osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture [3]. Osteoporotic cracks, for the most part, incorporate vertebrae, proximal femur, lower arm and proximal humerus. The quantity of breaks of the proximal femur is relied upon to increment fourfold by 2030. In the book "Bone Formation and Repair", published in '1994', W.C. Hayes declared: "If the prevalence of hip fracture continues to rise at current rates, it may well be that in the next few decades, orthopaedists will do little else but treat this problem". This explains, how much osteoporosis threatens the well – being and quality of life for women with postmenopausal osteoporosis.

There are a variety of factors involved in osteoporosis that can be classified into variable and constant factors, such as genetic factors and environmental factors. They could make a major contribution to the loss of bone mass contributing to osteoporosis, either individually or in synergy. Latest research studies suggest that factors associated with unhealthy living habits are also one of the most significant factors leading to postmenopausal women's rapid loss of bone mineral density.

Menopause results from a gradual decrease in ovarian function, resulting in low levels of ovarian-generated estradiol and other hormones. Some women develop moderate to severe symptoms at mid-life due to these hormonal changes. Many variables, such as menopausal status, lifestyle, geographic variation, and attitude towards menopause, can affect the frequency and severity of symptoms encountered by an individual woman.

Studies show that, general knowledge about bone health, daily dietary calcium intake, etc. is very low among Indian women. There was a study designed to find out about how much knowledge of osteoporosis is contained or known by educated women, and the researchers found out that, in general, the knowledge about osteoporosis was insufficient among women. So there arose a basic want or idea, for increased involvement of healthcare professionals like doctors, nurses, pharmacists, in education about bone health. Hence, calcium in low levels in the body, with existence of nutrient D insufficiency, in together have put a very deranged, sad information about osteoporosis, and drastically increasing cases of osteoporosis in India are a portion of the reasons that have brought about osteoporosis turning, into a significant general medical issue in India, particularly among the Indian women. As the incidence of bone fractures is increasing drastically in postmenopausal women affecting their health and quality of life, there is a need to create an environment of awareness in not only Indian women but also healthcare practitioners. Could there

be better management of postmenopausal osteoporosis in India? How can a cost-effective treatment be devised for women suffering from postmenopausal osteoporosis? Is there a possibility that lifestyle changes in early years can help avoid this? In this review article we aim to explore the various factors that put Indian women at risk for postmenopausal osteoporosis. We also aim to draw attention towards the lack of awareness related to this disease in India and different ways in which there can be better management of post-menopausal osteoporosis.

Epidemiology & Diagnosis of Postmenopausal Osteoporosis

Studies have now proven that there has been a rise in the life span of Indians. Also a disturbing rise of clinical osteoporosis has been noted in the number of women in India. While the information on the predominance of osteoporosis among ladies in India originates from examines directed in little gatherings spread the nation over, gauges propose that of the 230 million Indians expected to be beyond 50 2015 years old in 2015, 20% are osteoporotic ladies [4]. The lifetime risk of any fracture occurring in women from the age of 50 years is more than 40%. Refer to Figure 1.

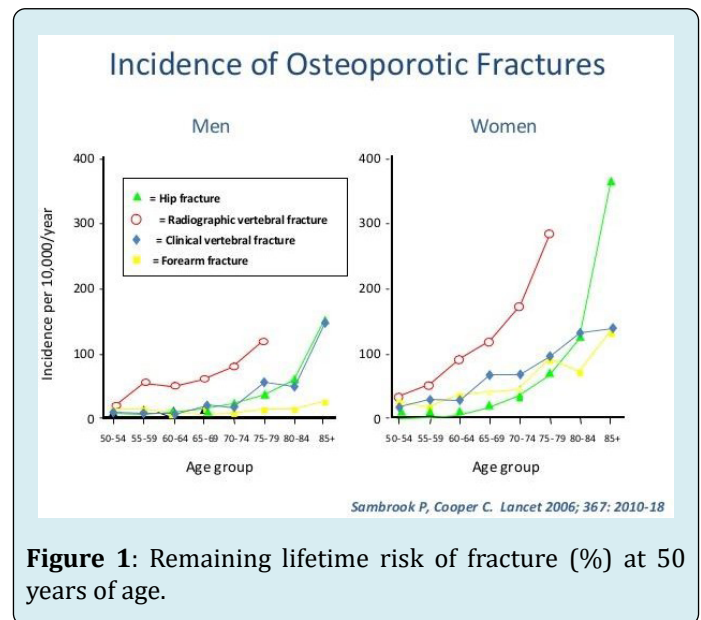


Figure 1: Remaining lifetime risk of fracture (%) at 50 years of age.

There is variety among people in the danger of crack at various locales at 50 years old. In ladies the leftover lifetime danger of any break at 50 years old years was 46.4% contrasted and only 22.4% for men. In ladies, the danger of hip crack was the most elevated, trailed by the lower arm, vertebral and proximal humerus breaks. In men, the example is comparative; however, there are more vertebral breaks than lower arm cracks.

If you conclude the studies conducted in India related to osteoporosis in women you'll find out that about 62% Indian women out of the whole population have shown signs and

symptoms of postmenopausal osteoporosis. The table below is a compilation of such different articles (Table 1).

Author/ Research Papers	The Main Study	Main Findings / Results
AS Babu [5]	N = 609(538 females, 71 males) Average age =52 yrs.[QUS]	Normal = 7.2 % Osteopenia = 40.6 %Osteoporosis =42.2 %
Paul TV [6]	N = 150(ambulatory postmenopausal women) Age = ≥ 50 yrs.[DXA]	Osteoporosis at: spine = 48 %,femoral neck = 16.7 %, at any site = 50 %
Sharma S [7]	N = 158 women Calcaneal [QUS]	b/w. 55-64 yrs.: Ope = 36.79 %; Opo = 20.25 % after 65 yrs:100%
Shatrugna V	N = 289women Age = 30 to 60 yrs [DXA]	Normal = 19 % Osteopenia = 52 % Osteoporosis = 29 %
Gandhi AB	N = 200 women Age = >40 yrs [DXA]	Age 40-65 yrs: Osteopenia = 34 %; Osteoporosis = 8 % Age > 60 yrs: Osteopenia & Osteoporosis = ~ 100 %
Aggrawal N	N = 500 postmenopausal women Mean age = 57 yrs [DXA]	Osteoporosis at hip = 15.8 %; Osteoporosis At spine = 28.6 % Age above 81 yrs: Osteoporosis in 66.7 %
Pande KC	N = 261 women Age = 50 to 79 yrs [Digital x-ray radiogrammetry]	Low bone mass = 50 %
Meeta [8]	N = 376 postmenopausal women [DXA]	Osteoporosis at Total hip = 4.2%; at spine = 22.07% Osteopenia at Total hip =17.82%; at spine = 35.11
Nikose	N = 3532 Mean age = 29.32 ± 9.8 [QUS]	Normal= 32.07% Osteopenic = 35.78% Osteoporotic =32,13%
Kaur	N = 250 post-menopausal women Age range = 45 to 80 yrs [DXA]	Osteoporosis = 26.4%
Shaki	N = 1400 peri- and post- menopausal women Age range= 23 to 50 yrs [QUS]	Osteoporosis in 81% Osteopenia in 19%

Table 1: Indian Studies on prevalence of osteoporosis.

“QUS”Quantitative Ultrasound,” DXA” Dual energy X-ray absorptiometry, “Ope” Osteopenia. “Opo”osteoporosis.

Postmenopausal osteoporosis is likewise possible to emerge as an extra common within side the many years in advance because of the lifestyles expectancy of the populace increases. The private and financial freight of post-menopausal osteoporosis effects from osteoporotic fractures, which might be a large public health problem, ensuing in considerable morbidity and mortality.

Osteoporosis can expand, if undetected, till a fracture occurs. Any bone may be affected, however fractures of the hip and backbone are of unique concern; hip fractures due to the fact they almost usually bring about hospitalization and most important surgery, main to impaired mobility that may be extended or permanent, and might even bring about death, whilst vertebral fractures can cause lack of height, intense backache, and deformity and also are related to increased mortality in Indian osteoporotic patients and have been accounted for to happen a whole lot sooner in Indians contrasted with individuals in the West (Figure 2). The Delhi Vertebral Osteoporosis Study (DeVOS) revealed a

predominance of 17.1% of vertebral breaks among the 415 females subjects (age >50 years) joined up with the study [9]. Hip crack rates were accounted for to be 159/100,000 ladies beyond 50 years old years in Rohtak region, North India [10].

Bone strength	Genetic make-up
	Nutrition
	Physical activity
	Body weight
Bone loss	Age
	Menopause - estrogen deficiency
	Smoking
	Alcohol
	Late menarche
	Low bone mass - sarcopenia
	Premature ovarian failure

Figure 2: Factors determining Bone Strength & Bone Loss.

Pathogenesis

Some of the main reasons for a fragile skeletal system can be because:

- When the body fails to form a skeleton that contains the right amount of mass and strength during growth
- When there is a gradual decrease in bone mass leading to deterioration of the skeletal system mainly due to excessive bone resorption
- Due to inadequacy in formation of bones cause of drastic bone resorption phenomena during bone remodeling

Estrogen deficiency to begin with, proposed to be the only mechanism via way of means of which bone mass decreases in postmenopausal women and aged men. The pathways worried in this encompass the differential consequences of

estrogen on osteoblast/ osteoclast apoptosis, inflammatory cytokine-mediated growth in osteoclast, and hobby and absence of estrogen-brought on suppression of hypoxia-inducible element 1 alpha protein, main to osteoclast activation [11]. However, current research display that growth in follicle-stimulating hormone ranges additionally contributes to the imbalance among bone formation and resorption via way of means of messenger RNA expression of genes consisting of receptor activator of nuclear element kappa B (RANK), tartrate-resistant acid phosphatase, matrix metalloproteinase-9, and cathepsin K in a dose-dependent manner, thereby growing osteoclastic hobby [12]. Figure 3 below depicts the pathogenesis of postmenopausal osteoporosis [13].

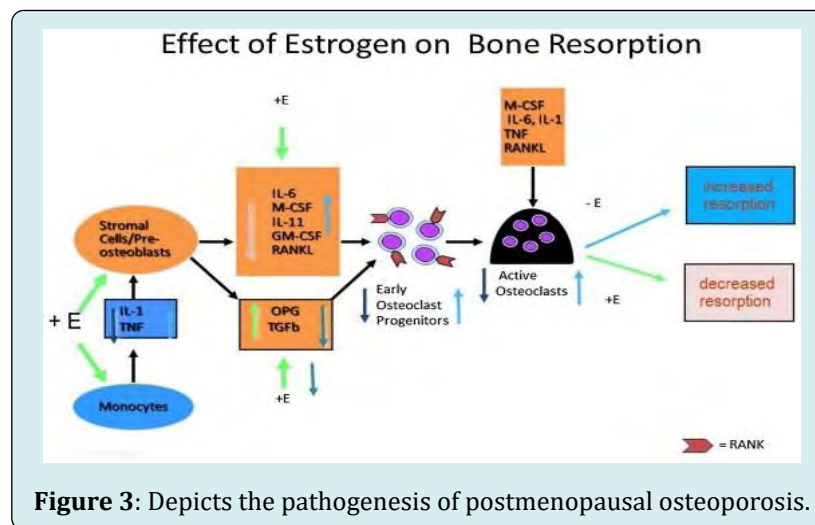


Figure 3: Depicts the pathogenesis of postmenopausal osteoporosis.

Risk Factors and Causes of Postmenopausal Osteoporosis

Various elements are worried within side the etiology of osteoporosis amongst Indian women. The non-modifiable elements consist of – “sex, advancing age, ethnicity, and genetic elements”. Women whose body frame are smaller in size, are much more expected to have decreased quantities of calcium-wealthy ingredients and for socio-cultural motives are possibly to have terrible daylight publicity. Further, estrogen being crucial for the development & growth of bone in ladies, reduced intervals of exposure to estrogen all through a woman’s lifetime might also additionally make contributions in a first-rate manner to the improvement of osteoporosis [14]. Though the common age at menarche in Indian ladies is 12.5 years, age at menopause is frequently in advance than that visible in Caucasian ladies [15]. This has been mentioned to be a big threat thing for the improvement of osteoporosis in Indian women [16]. Numerous research have mentioned the growing occurrence of osteoporosis with advancing age, and this fashion was discovered to a

terrific quantity amongst Indian ladies than men.

Genetic elements, race, & ethnicity additionally have completely sturdy impact on height bone mass. Asian Indian ladies were proven to have decreased BMD than their Caucasian and Black counterparts [17].

Evaluation for Osteoporosis

Assessment of osteoporosis includes evaluation of risk factors that may adversely affect bone health, biochemical assessment, radiological imaging, and fracture risk assessment tools. The dangerous elements that result in bone loss were defined already.

Biochemical Assessment

Biochemical assessment includes albumin-corrected overall serum calcium, phosphate, alkaline phosphatase, creatinine, 25-hydroxyl vitamin D (now no longer mandatory), and parathyroid hormone (PTH) (in decided on cases). In

addition, in decided on cases, secondary reasons along with Cushing syndrome, number one hyperparathyroidism, and a couple of myelomas want to be dominated out.

Bone Turnover Markers

Bone turnover markers (BTMs) are biochemical markers used for the assessment in addition to the tracking of remedy for osteoporosis. They are dependable and cost-powerful in maximum scientific settings. Bone remodelling is maintained with the help of a process, in which there is coupling of formation of the bone and resorption at diverse timelines, which leads to non-stop transforming of bone. Studies related to this topic show the dynamics of bone remodelling in lots of metabolic bone problems primarily based totally at the growth or lower within side the bone formation/resorption markers. They are beneficial within side the estimation of fracture danger and tracking the adherence and reaction to therapy. However, the BTMs are subjected to diverse pre-analytical and analytical versions of strict pattern series and assay strategies at the side of utilizing ethnicity-primarily based totally reference requirements for unique populations [18]. Biochemical markers of bone metabolism are widely divided into markers of bone formation and markers of resorption.

Dual-Energy X-Ray Absorptiometry Scan

BMD evaluation via way of means of (DXA) i.e. Dual-energy X-ray absorptiometry experiment (Figure 4) is the gold standard, for analysis of osteoporosis. It offers an estimate of the amount of bone gift at numerous websites and is the usual degree for osteoporosis. It is an exceedingly correct X-ray method used for the dimension of BMD at skeletal web sites which includes lumbar spine, hip, and wrist. Bone BMD measured via way of means of DXA is expressed as g/cm^2 . However, via way of means of the convention, the rating then is transformed to a T-rating and a Z-rating.

- T-rating: Refers to the number of popular deviations below or more than the Bone Mineral Density of matched controls, according to their age.
- Z-rating: Refers to the number of popular statistics above or below the basic Bone Mineral Density of the younger everyday geometric mean.

According to World Health Organization criteria, osteoporosis is defined as T-score ≤ -2.5 (Table 2). Z-score of ≤ -2 is defined as low bone mass or bone mass below the expected range for age (this term is used in women).

Definition	Score
Normal	T-score above (i.e., better than) -1.0
Osteopenia or low bone mass	T-score between -1.0 and -2.5
Osteoporosis	T-score below (i.e., worse than) or equal to -2.5
Severe osteoporosis	T-score below -2.5 with fragility fracture

Table 2: Low bone mass or bone mass below the expected range for age.

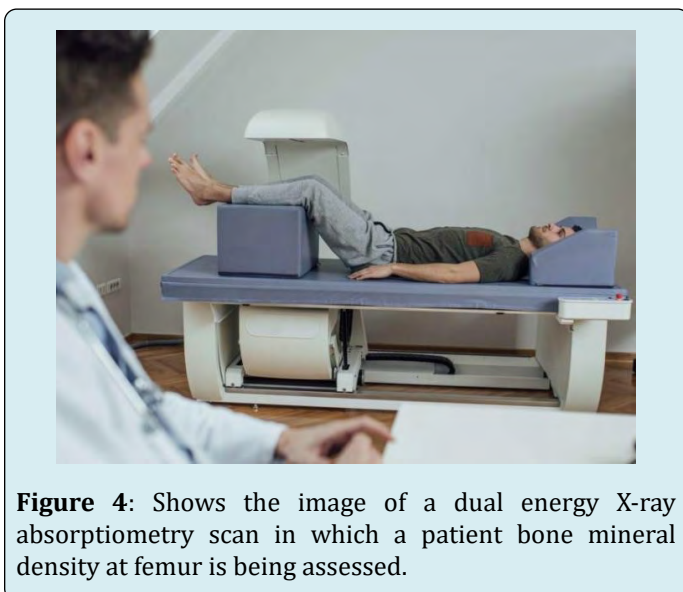


Figure 4: Shows the image of a dual energy X-ray absorptiometry scan in which a patient bone mineral density at femur is being assessed.

Limitations of Dual-Energy X-Ray Absorptiometry Scan

Although BMD is presently the gold well-known degree of osteoporosis, many sufferers with fractures are discovered to have BMD in the osteopenia/ordinary range [19]. Thus, an ordinary BMD cannot rule out the opportunity of osteoporotic fracture. In addition, notwithstanding BMD getting used as a degree of assessment of remedy efficacy in medical practice, research has proven that there's a terrible correlation between the growth in BMD with antiresorptive remedy and the volume to which the remedy decreases fracture risk [20]. In India, the quantity of DXA scanning facilities is constrained and a maximum of them are positioned in city areas.

Fracture Risk Assessment Tool (FRAX)

FRAX is the most broadly used fracture risk evaluation device that takes under consideration 9 elements, specifically

age, BMD, body mass index (BMI), earlier fragility fracture, use of oral glucocorticoids, parental records of HF, modern smoking, alcohol intake, and rheumatoid arthritis (Figure 5). It predicts the 10-yr probability of HF and major osteoporotic fracture (MOF) [21]. A threshold of >20% for MOF and >3% for HF is taken into consideration the intervention threshold for beginning for osteoporosis.

The major goal of the usage of the FRAX device is to permit scientific experts to become aware of the ones sufferers

who could gain from pharmacological remedy in lowering fracture danger. However, like another medical device, FRAX has few limitations. It does not no longer embody all of the crucial elements which can expect fracture danger in a given person consisting of bodily activity, Vitamin D deficiency, chances of all evaluation, BTMs, or the price of bone loss on sequential BMDs. FRAX additionally wishes validation for determining thresholds (of MOF and HF) primarily based totally on ethnicities [22].

Figure 5: The image shows the web-based FRAX tool.

Who to Screen for Osteoporosis?

The following patients want to be screened for osteoporosis via way of means of DXA primarily based totally on the advice via way of means of the Indian Menopause Society (IMS) [23]

- All postmenopausal girls more than five years of menopause
- Postmenopausal girls <5 years of menopause with risk factors

(Low BMI, glucocorticoid use, alcohol, smoking, rheumatoid arthritis, previous records of fragility fracture, and parental records of HF)

- Menopausal women that are transitioning with secondary reasons
- When a proof as per radiology for - osteopenia and/or presence of - vertebral compression fracture is noticed
- Women suffering with fragility break or fracture
- Earlier ideally, before beginning pharmacotherapy for

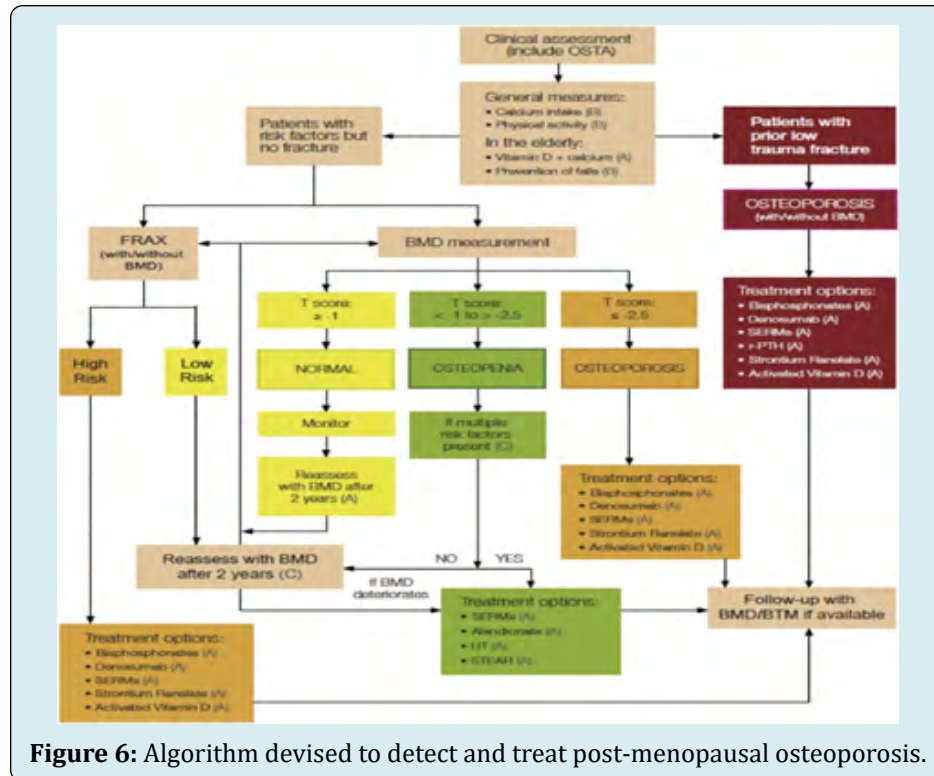
women detected with osteoporosis.

Who to Treat for Osteoporosis?

According to the IMS, the remedy of osteoporosis is indicated within side the following situations:

- Presenting with fragility fractures
- On the diagnosis of osteoporosis that is mainly based on results after DXA scan, i.e., T- score ≤ -2.5 for areas of hip, spine along with other reasons & more risk of fractures
- In the absence of Bone Mineral Density measurements via way of means of DXA, for treating postmenopausal women, intervention is individualized, knowledge and thinking about the value gain and chance gain results of the intervention.

This flowchart below is an algorithm devised to detect and treat post-menopausal osteoporosis.



Awareness About Post-Menopausal Osteoporosis Among Women:

Osteoporosis reasons the bones to be fragile and will increase susceptibility to fracture in spite of trivial trauma. Prevalence of osteoporosis in apparently healthy adults above 40 years of age in Pune City, India [42] after attainment of menopause in women, the manner of osteoporosis is elevated with the aid of using estrogen deficiency. Estrogen facilitates in retaining (Figure 6) nice calcium stability and in osteogenesis.

Menopause speeds up the fee of bone loss with the aid of using 2%–5% in line with year, and this could keep for the subsequent 10 years. In a current study, the superiority of osteoporosis in ambulatory postmenopausal girls becomes proven to be 50% at any site. The 1-12 month's mortality after osteoporotic hip fractures is envisioned to be approximately 20% [6]. The fundamental requirement for coping with any persistent fitness disease begins off evolved with assessment of the notice approximately the ailment a few of the goal subjects.

Although an awesome expertise of the ailment won't be enough to result in modifications in fitness-associated behaviour, good enough know-how is a prerequisite for the fulfillment of preventive efforts. There is proof suggesting that know-how approximately osteoporosis is a contributor to osteoporosis preventive behaviour, even

though this isn't always a clear-reduce relationship. In India, attention of osteoporosis is low, seeing that there was surprisingly little attempt to publicize the ailment. Although few surveys indicate that recognition approximately the disorder within side the city populace is inadequate, there aren't any large-scale surveys undertaken to evaluate the intensity of recognition and expertise of osteoporosis in postmenopausal girls. Since osteoporosis is a giant hassle in Indian postmenopausal girls with giant growth in morbidity and mortality following fragility fractures, it's far in reality vital that they be screened pre-emptively for the presence of osteoporosis. Very often, screening efforts are hampered via way of means of the lack of knowledge of this circumstance amongst rural postmenopausal subjects. To sell expertise and higher fitness searching for conduct amongst postmenopausal girls, it's far important to evaluate their present day country of recognition and paintings in the direction of decreasing the diagnosed gaps in expertise. The effects of this look at are applicable for own circle of relatives and number one care physicians in addition to for coverage makers to behaviour applications periodically to initiate the notice amongst postmenopausal girls concerning osteoporosis. Hence, this look at became achieved to evaluate the notice of osteoporosis amongst postmenopausal girls, attending a coaching sanatorium in southern India. The look at achieved the use of a formerly confirmed questionnaire-primarily based totally tool (Figure 7) Osteoporosis knowledge assessment tool (OKAT).

Items	Correct answer	% of correct answer (No.)
1. Osteoporosis leads to an increased risk of bone fractures.	True	77.4 (234)
2. Osteoporosis usually causes symptoms (e.g., pain) before fractures occur.	False	8.6 (26)
3. Having a higher peak bone mass at the end of childhood gives no protection against the development of osteoporosis in later life.	True	21.8 (66)
4. Osteoporosis is more common in men.	False	46.3 (140)
5. Cigarette smoking can contribute to osteoporosis.	True	33.4 (101)
6. White women are at highest risk of fracture when compared with other races.	True	22.51 (68)
7. A fall is just as important as low bone strength in causing fractures.	True	58.2 (176)
8. By age 80 years, a majority of women have osteoporosis.	True	62.5 (189)
9. From age 50 years, most women can expect at least one fracture before they die.	True	34.1 (103)
10. Any type of physical activity is beneficial for osteoporosis.	False	39.7 (120)
11. It is easy to tell whether I am at risk of osteoporosis by my clinical risk factors.	True	46.0 (139)
12. Family history of osteoporosis strongly predisposes a person to osteoporosis.	True	41.0 (124)
13. An adequate calcium intake can be achieved from two glasses of milk a day.	True	65.5 (198)
14. Ragi and broccoli are good sources of calcium for people who cannot take dairy products.	True	45.0 (136)
15. Calcium supplements alone can prevent bone loss.	False	26.4 (80)
16. Alcohol in moderation has little effect on osteoporosis.	True	32.8 (99)
17. A high salt intake is a risk factor for osteoporosis.	True	34.4 (104)
18. There is a small amount of bone loss in the 10 years following the onset of menopause.	False	6.7 (20)
19. Hormone therapy prevents further bone loss at any age after menopause.	True	28.4 (86)
20. There are no effective treatments for osteoporosis available in India.	False	13.2 (40)

Figure 7: OKAT questionnaire.

The reason for the study was to evaluate the extent of awareness of osteoporosis amongst postmenopausal women attending a coaching health center in southern India, specifically in regards to danger elements, remedy options, and results. The reason for choosing postmenopausal women as observe individuals changed into that they're at the best danger for osteoporosis and fragility fractures, and this warrants early and pre-emptive screening on this group. In this observation, the implied age of attainment of menopause changed into forty-six years. This is regular with the observations carried out with the aid of using Ahuja, et al. [24] wherein the common age of menopause of an Indian girl changed into forty six.2 years [25]. The median age at menopause amongst white ladies from industrialized international locations stages among 50 and 52 years [26-29]. Earlier menopause is related to an accelerated danger of osteoporosis and fragility fractures. This underscores the want for the well-timed screening of postmenopausal ladies and early initiation of remedy to save you the prevalence of fractures.

To the quality of our understanding, that is the primary observation from south India to evaluate recognition concerning osteoporosis, amongst a cohort of postmenopausal ladies referred for DXA scan. Overall, it changed into discovered that the knowledge approximately osteoporosis, its danger elements, and remedy changed into bad on this cohort. In a comparable observe achieved in one hundred postmenopausal ladies, there has been an amazing deficit in understanding concerning osteoporosis and its prevention [29-33].

The grossly insufficient country of recognition in regards to osteoporosis mandates that remedial measures be followed to bridge this hole in understanding [33-35]. The individuals of our observation had a bad understanding approximately the danger elements and the results of osteoporosis and simplest 13% have been conscious that powerful remedies for osteoporosis existed in India.

This unluckily displays the large lacunae in the knowledge of the disabling results of osteoporosis, its danger elements, and remedy. On evaluating the overall performance of individuals stratified in step wFith their academic status, no large distinction changed into determined among illiterate/number one stage knowledgeable and the relaxation of the individuals in regards to osteoporosis recognition [36-40]. A small survey carried out in western India has proven media to be the maximum not unusual place supply of facts on osteoporosis and simplest 1 / 4 of the topics recognized medical doctors as a supply of facts. This well-known shows the truth that with the contemporary gadget of schooling, the burden of significance given to osteoporosis and its results might be suboptimal.

This requires the initiation of tutorial ventures as a way to decorate recognition approximately osteoporosis and its remedy. Family physicians who offer number one care to the aged have to talk approximately osteoporosis in the course of health facility visits for control of continual illnesses consisting of diabetes or hypertension.

Conducting osteoporosis recognition applications in faculties and faculties will help in enhancing their

understanding on this regard [41]. Utilizing mass media consisting of print, broadcast, and virtual media to enhance recognition will assist in achieving out to a majority of the overall public. Individuals susceptible to osteoporotic fractures that attend hospitals for different illnesses maybe supplied with facts leaflets approximately osteoporosis and fall prevention. Primary care physicians need to prioritize on designing suitable fitness schooling techniques for people at accelerated danger of osteoporosis primarily based totally on their stage of literacy.

Osteoporosis recognition applications at the mass media in nearby languages could attain a massive share of people.

Management of Postmenopausal Osteoporosis

Lifestyle Modifications

A. Dietary calcium: Calcium enables preserving the strength and shape of bones. Calcium is available in the maximum of the dairy products. The recommended day by day allowance of calcium is 1000-1500 mg. Much Indian research has proven that our nutritional calcium consumption is properly beneath the advocated amount. In a cross-sectional look from South India, 74.5% of the postmenopausal girls have been ingesting much less than the advocated day by day allowance of calcium.

- B. Physical activity:** Reduced physical activity is a major risk factor for the development of osteoporosis and fractures. Moderately increased physical activity, which is done regularly for long-term periods, helps in improving the mechanical competence of the skeletal system considerably.
- C. Fall prevention:** Elderly people are more prone to fall because of poor eye sight, loss of coordination, and development of neuropathy. They should be aware of the fall preventive measures such as, using hand rails for going up and down the steps, avoid walking in slippery surfaces and using a walking stick if needed.
- D. Calcium and cholecalciferol:** Calcium and Vitamin D supplements are considered a first-line treatment in osteoporosis. Various calcium preparations are available in our country. Calcium carbonate needs acid for its absorption. In patients who are taking drugs which reduce gastric acid secretion, it is advised to give calcium citrate maleate. Vitamin D supplementation in the form of cholecalciferol is considered one of the early treatments in osteoporosis (Table 3). Vitamin D deficiency is prevalent in 70% of the general population in our country [8,42]. Cholecalciferol 60,000 U once in every 1-2 months is recommended in all postmenopausal women with or without osteoporosis. Active Vitamin D (calcitriol) is not indicated in the usual management of osteoporosis unless patients have renal dysfunction. The table below is a collection of Indian foods that have rich calcium content (Table 4).

S.No	Dietary Product	Serving	Calcium(Mg)
1	(Buffalo) Milk, Curd	250ml	520
2	Milk, Curd(Cow)	250ml	300
3	Milk, Curd(Low Fat)	250ml	300
4	Khoa	100gms	600
5	Paneer	100gms	320
6	Cheese Slice	20gms	160
7	Ragi	100gms	360
8	Horse Gram Whole	100gms	270
9	Soyabean	100gms	240
10	Moth Bean/Bengal Gram	100gms	200
11	Rajma	100gms	260
12	Red/Green/Black Gram (Whole)	100gms	100
13	Chickpea/Kabuli Chana	100gms	120
14	Drum Stick Leaves/Parsly	100gms	300
15	Radish Leaves/Methi Leaves	100gms	270

Table 3: Indian Foods with Calcium (Ca) Rich Content.

Class of Women	Ca In Mg
Adult Women	600
Pregnant women	1200
Women during Lactation	1200
Postmenopausal	800

Table 4: Recommended Dietary Allowance of Ca (Calcium).

Pharmacotherapy

Drugs used for the treatment of osteoporosis are widely divided into antiresorptive and anabolic agents.

Antiresorptive Agents

The classification of anti-osteoporotic drugs is shown in Figure 8.

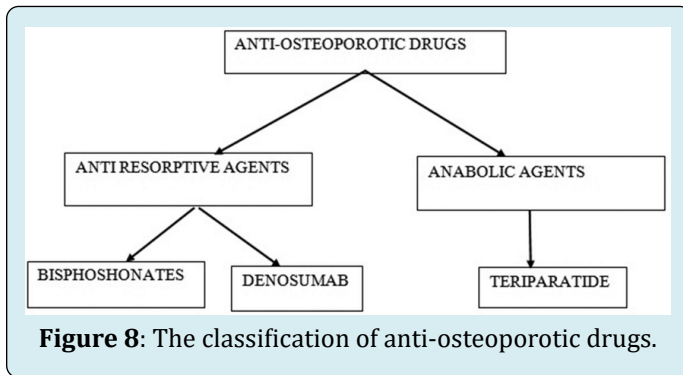


Figure 8: The classification of anti-osteoporotic drugs.

Bisphosphonates

Bisphosphonates are the class of drugs that have been used in the treatment of osteoporosis in a lot of cases.

First line medications	Effect on vertebral fracture risk		Effect on non-vertebral fracture risk	
	Osteoporosis	Established osteoporosis*	Osteoporosis	Established osteoporosis*
Alendronate	+	+	NA	+(including hip)
Risedronate	+	+	NA	+(including hip)
Zoledronate	+	+	+	+
Ibandronate	NA	+	NA	+^

Table 5: Efficacy of Anti-fracture first line bisphosphonates for PMO, when administered with vitamin D and calcium supplements. (Rizzoli 2004) 'NA' no evidence available; '*' Women with prior vertebral fracture; '^' in subsets of patients only (post-hoc analysis).

Effective care of patients at elevated fracture risks includes appropriate examination and a well-planned and

developed treatment procedure, keeping in compliance with the dosing protocols.

Data suggest that osteoporosis patients with successful long term compliance with treatment experience notably lower chances of fracture. Persistent care also correlates to improved BMD and improved bone resorption and replacement marker suppression. While bisphosphonates are the most effective anti-resorptive agents currently approved, they have Unique dosing problems that can have contradictory effects on long term persistence (Table 5). The difficulty of certain dosing requirements; the potential for adverse effects, particularly when the instructed doses are not followed; and very low absorption rates all lead to poor results, even under ideal conditions. The expansion of the dosage period from a once per day to a once in a week regimen is associated with comparable effectiveness, can potentially increase the protection of the gastrointestinal tract, and also associates with a major upgradation in therapy persistence.

Contraindications for Bisphosphonates

- Chronic kidney disease (estimated glomerular filtration rate).
- Suppressed bone turnover beta cross-Laps (CTX) Severe allergic reaction to previous bisphosphonate therapy.

Side Effects of Bisphosphonates

- Gastrointestinal toxicity, related to oral bisphosphonates.
- Acute-phase reaction – Fever, chills, and body pain, related to IV bisphosphonate.
- Atrial fibrillation.
- Electrolyte imbalance – Hypocalcaemia, hypomagnesaemia, hypokalemia, and hypophosphatemia.
- Related to long-term therapy -
- Excessive suppression of bone remodelling leading to increased bone fragility
- Atypical fractures – Low-energy subtrochanteric femoral fractures. These are often preceded by prodromal thigh pain
- Osteonecrosis of the jaw. Some examples are-
- Risedronate (Actonel)

- Alendronate (Fosamax)
- Ibandronate (Boniva)
- Zoledronic Acid (Reclast)

Denosumab

Denosumab is another potent antiresorptive agent which acts by inhibiting RANK ligand, thus preventing proliferation and maturation of pro-osteoclasts. It is given as subcutaneous injections once in every 6 months. This drug can be used even in patients with chronic kidney disease Stage 3 or above. It is a monoclonal antibody for osteoporosis, recently approved in India. It is given as subcutaneous injections, 60mg, once in every 6 months. It increases the cortical and cancellous bone strength, and also increases BMD, more effectively than bisphosphonates. It has good patient compliance and also is cost effective. This medication is recommended in cases of high risks of osteoporotic fractures. This drug can be prescribed even in cases of chronic renal disorders as it is finely tolerated in patients with creatinine clearance <30 ml/min [8]. The outcomes of this therapy can rebound after 6 months if the dose is not taken on time, and so any interruption or delay or termination in treatment is not recommended, especially without a subsequent antiresorptive. Thus, considering the rebound activity and to prevent it, the Swiss association guidelines have made the subsequent administration of alendronate or zoledronic acid for 2 years compulsory, initiating it 6 months from the last administration of denosumab.

ADE-Skin rash or eczema, hypocalcaemia, and over suppression of bone turnover are some of the side effects of denosumab therapy.

Example

Prolia: Contrasted and week after week organization of alendronate (Fosamax), denosumab essentially

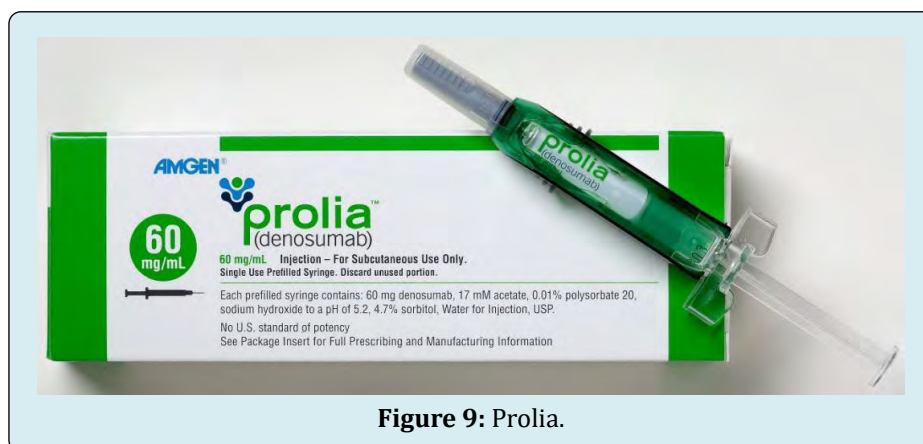


Figure 9: Prolia.

Expands bone mineral thickness in postmenopausal patients with low bone mass. Three among post-menopausal women who had taken alendronate for at least half year, those changed to denosumab altogether expanded bone mineral thickness at one year versus the individuals who kept accepting alendronate. But, the principle motivation behind why Prolia is being dodged on the market grounds is, that it costs \$1,980, i.e. 145878.58 in rupees, for one year of treatment, in addition to doctor's or medical staff's expenses for organization, in order to observe calcium, phosphorus, (Figure 9) and magnesium levels. All this factors makes Prolia more costly than oral or intravenous bisphosphonates.

Selective Oestrogen Receptor Modulators (SERMs)

Although the Hormone Replacement Therapy (HRT) did provide protection and relief to women dealing with postmenopausal osteoporosis, but along with that, it also brought some undesirable complications in the form of breast and endometrium cancer. Hence, the need for such a treatment that avoids these undesirable effects on other

organs resulted in the development of Selective Estrogen Receptor Modulators (SERMs). SERMs are a class of drugs that inhibit bone resorption without any side effects on the endometrium and breast.

They are non-steroidal, chemically synthetic in nature. SERMs wield an anti-estrogen effect in the breast and endometrium of the uterus, whereas in the bone, they exert an estrogen agonist effect. SERMs (eg. Raloxifene) processes small surge in the BMD in comparison to other treatments but, lessens the chance of vertebral fractures by 36%. However, there is insufficient evidence for its effect on hip and no vertebral fractures, and its efficacy is lower than that of other antiresorptives. This treatment is preferably given to patients who have low risk of deep vein thrombosis; otherwise a condition of venous thromboembolic can persist. Also the ones who are at a high risk of breast cancer are prescribed SERMs (Table 6). The most frequently used drugs for SERMs, at present, are bazedoxifene and raloxifene. SERMs has proved to be a great help in lowering new vertebral fracture risk by 69% in postmenopausal women with osteoporosis over 3 years, which parallel has shown decrement by 76% in the risk of invasive breast cancer [8].

Drug	Endometrium	Breast	Bone	Lipids
Toremifene	+	-	+	+
Tamoxifen	+	-	+	+
Raloxifene	-	-	+	+
Estradiol	+	+	+	+

Table 6: Effects Of FDA approved SERMs on specific tissues

Calcitonin

Calcitonin acts by inhibiting bone resorption by increasing osteoblast activity. To date, data on the effect of calcitonin on BMD of other skeletal sites are conflicting, as shown in recent studies. Hence, it is not recommended for the treatment of osteoporosis.

Anabolic Agent

➤ **Teriparatide:** Teriparatide is a recombinant human PTH (1-34) which is administered as subcutaneous injections daily (20 µg/day). The total duration of treatment ranges from 18 to 24 months. Cost is a major concern in PTH therapy. As teriparatide increases both bone formation and resorption, it is advised to give bisphosphonates after completing the course of PTH therapy.

Indications for teriparatide

- Multiple vertebral fractures (clinical or radiographic)
- Very low BMD (T-score <-3)
- Suboptimal response to antiresorptive therapy (incident fractures or active bone loss during therapy)

Newer drugs in anti-osteoporotic therapy

- Abaloparatide
- Romosozumab.

Using anabolic and antiresorptive agents in combination or in succession improve bone density and bone strength more than either agent alone due to their synergistic action. (Table 7) this is called combination/sequential therapy and is useful in selected cases.

Drug	Dosa Ge	Route	Position In Therapy	Vertebral*	Hip*	Non- Vertebral*	Precautions	Advantages	Disadvantages	Contra-Indications	Adverse Effects
CALCITONIN	200 IU daily	Nasal Therapy	2 nd line	Yes, 21 %	No	No	Serious hypersensitivity reactions, including fatal anaphylaxis	Ease of administration	Circulating antibodies to calcitonin-salmon may develop, and may cause loss of response to treatment	Hypersensitivity to calcitonin-salmon	Rhinitis, Epistaxis, and Allergic reactions,
TIBOLONE	2.5 mg daily	Oral	1st line	Yes, 50 %	Yes, 26 %	Yes, 26 %	drug interaction with Warfarin	Increases BMD, decreases cholesterol and triglycerides	Reduction of HDL levels and its high cost	Pregnancy and lactation, Breast cancer, Oestrogen dependent malignant tumours, Hypersensitivity to the active substances, Porphyria	Vaginal discharge, Endometrial wall thickening, Postmenopausal haemorrhage, Breast tenderness, Genital pruritus, Vaginal candidiasis, Vaginal haemorrhage, Abnormal hair growth, Lower abdominal pain
RALOXIFENE	60 mg every daily	Oral	At risk of breast cancer, < 10 yrs menopause	Yes, 40 %	No	No	With a low risk of deep vein thrombosis, in case bisphosphonates or denosumab are not appropriate, or with a high risk of breast cancer.	reduced incidence of invasive estrogen receptor positive breast cancer	Daily oral administration	Pregnancy, lactation, Active history of thromboembolic disorders	Venous thromboembolism, Stroke, Myocardial infarction, Cancer (breast, endometrial, ovary), Dementia, Gallbladder disease, and Urinary incontinence
DENOSUMAB	60 mg every 6 months	SC	1st line	Yes, 68 %	Yes, 40 %	Yes, 20 %	Hypocalcemia, Vit D status, Pregnancy, Lactation, Pediatric	1st line drug, can be used in patients in eGFR 15-30 ml/min	Loss of effect after discontinuation	Hypocalcemia, Hypersensitivity	Dermatitis, Rash, Mild bone/Muscle pain, UTIs

TERIPARATIDE	20 mcg daily SC	SC	For severe osteoporosis	Yes, 65 %	Insufficient data	Yes, 53 %	Hypocalcaemia, Vitamin D status, Hypersensitivity, Local tissue damage, Pregnancy, Lactation, Pediatric	Potent bone forming activity, Large increase in spine BMD over 2 years	Reserved line drug, 2 years usage, daily injections required	Hypocalcaemia, Hypersensitivity	Headache, Hypercalcaemia, Hypercalciuria, Renal adverse effects, Nausea, Rhinitis, Arthralgia
RISEDRONATE	5 mg daily; 35 mg weekly; 150 mg monthly	Oral	1st line	Yes, 41-49 %	Yes, 30 %	Yes, 36 %	should not be used in patients with eGFR below 30 ml/min, Pregnancy, Lactation, Paediatric		Inconvenient administration- stay uptight for 30 mins on intake, no food before drug consumption, drug holiday may be needed 3-5 years	Hypocalcaemia, Hypersensitivity, Compromise of renal function, Upper GI disease, patients at increased risk of aspiration	Rash, Abdominal pain, Dyspepsia, Diarrhoea, Arthralgia
ALENDRONATE	5/10mg daily; 35/70mg weekly; 150mg monthly	Oral	1st line	Yes, 50 %	Yes, 51-56 %	Yes, 49%	should not be used in patients with eGFR below 30 ml/min, Pregnancy, Lactation, Paediatric	Most commonly used drug	Inconvenient administration- stay uptight for 30 mins on intake, no food before drug consumption, drug holiday may be needed 3-5 years	Hypocalcaemia, Hypersensitivity, Compromise of renal function, Upper GI disease, patients at increased risk of aspiration	Dyspepsia, Esophagitis abdominal pain, Musculoskeletal

Table 7: Common medications used in Osteoporosis Therapy.

Monitoring and Follow-up

Those who are on anti-osteoporotic treatment should be monitored for side effects of the drugs. It is very important to decide the frequency and duration of the treatment for each patient according to their response to therapy. BTMs (if available) can be monitored once in every 3–6 months, BMD by DXA once in every 1–2 years, and X-ray spine and hip – if clinically indicated. It is important to screen for atypical femur fracture in any patient on bisphosphonate therapy who presents with thigh pain. Drug holiday – in patients who are on antiresorptive therapy, it is advisable to withhold treatment if the bone turnover is suppressed.

Conclusion

As per the various studies conducted over the last few years it's now clear that there is a gradual increase of postmenopausal osteoporosis in women all across the globe especially India. Hormone Replacement Therapy (HRT)

cannot be taken as a permanent or definitive solution to this crippling disease due to higher risk/benefit ratio making it unfavourable. A lot of patients with even fragility fractures aren't tested properly these days leading to disability or even death. Therefore it's highly important that with the help of global organizations and country based ones multipronged approach involving education intervention, lifestyle modification, fall prevention, appropriate pharmacotherapy for the patients, campaigns and awareness be spread regarding the prevention and treatment of PMO among people especially women. If this issue is addressed soon it can help avoid the threat imposed on the quality of life of a women suffering from postmenopausal osteoporosis and also remove a major burden on the economy.

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