Review Article

Thyroid disorders and bone mineral metabolism

Dinesh Kumar Dhanwal

Department of Medicine, Maulana Azad Medical College, New Delhi – 110 002, India

ABSTRACT

Thyroid diseases have widespread systemic manifestations including their effect on bone metabolism. On one hand, the effects of thyrotoxicosis including subclinical disease have received wide attention from researchers over the last century as it an important cause of secondary osteoporosis. On the other hand, hypothyroidism has received lesser attention as its effect on bone mineral metabolism is minimal. Therefore, this review will primarily focus on thyrotoxicosis and its impact on bone mineral metabolism.

Key words: Bone metabolism, bone mineral density, hyperthyroidism, hypothyroidism, India, thyroid disorders

Thyrotoxicosis and Bone

Hyperthyroidism is a common endocrine disorder and Graves' disease is the commonest cause of thyrotoxicosis. Patients with active Graves' disease have widespread systemic manifestations involving all organ systems such as CNS, respiratory, cardiovascular, reproductive, gastrointestinal and skeletal system. The effects are due to the metabolic actions of excess thyroid hormones. Vitamin D deficiency is widely prevalent throughout the world including India.[1] Recently, Dhanwal *et al.* have reported hypovitaminosis D and its impact on bone mineral homeostasis and bone density.[2] Patients with Graves' disease in India have steatorrhea and marked proximal muscle weakness due to skeletal muscle myopathy.[3] Majority of patients have increased skin pigmentation during thyrotoxic state.[4] Thyroid hormones have direct catabolic effect on bone mineral homeostasis, leading to increased bone mineral resorption and calcium loss through kidneys.[5] Increased skin pigmentation and related vitamin D deficiency coupled with excessive urinary calcium loss, caused by thyrotoxicosis, may well be responsible for causing significant abnormalities in bone mineral homeostasis in thyrotoxic patients in India. Negative calcium balance due to catabolically induced increase in bone resorption may also be operative in Indian thyrotoxic patients.

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.83339

Regulation of Normal Bone Mineral Homeostasis

Bone mineral homeostasis is predominantly controlled by three hormones, i.e. parathyroid hormone (PTH), $1,25(OH)_2D$ and calcitonin.[6] These hormones act on three target tissues, i.e. bone, intestine and kidney. There is a close interaction among PTH, $1,25(OH)_2D$ and calcitonin to regulate serum calcium, phosphorous, and magnesium levels through actions on target tissues. In skin, ultraviolet light (wavelength of 290–315 nm) converts 7-dehydrocholestrol, a precursor of cholesterol, to vitamin D_3. Vitamin D_3 is metabolized in the liver to 25(OH)D by 25-hydroxylase enzyme and then in kidneys to its active form $1,25(OH)_2D$ by 1-αhydroxylase enzyme. Serum 25(OH)D has a longer half-life of 21 days and is a measure of vitamin D nutritional status. $1,25(OH)_2D$ stimulates calcium absorption in gut and also regulates bone turnover and renal excretion of calcium and phosphorous.[7] The net effect of $1,25(OH)_2D$ is to raise serum calcium while decreasing PTH. Serum calcium and $1,25(OH)_2D$ levels regulate PTH secretion from parathyroid gland. PTH stimulates bone turnover and renal phosphorous excretion

Corresponding Author: Dr. Dinesh Kumar Dhanwal, 115, B. L. Taneja Block, Maulana Azad Medical College, New Delhi – 110 002, India.
E-mail: dineshdhanwal@hotmail.com

by inhibiting phosphorous reabsorption in proximal and distal tubules and renal calcium reabsorption at distal tubule. The net effect of PTH is to raise serum Ca and $1,25(OH)_2D$ while decreasing serum phosphorous levels.

Normal Bone Remodeling

Bone remodeling is a dynamic process and characterized by coupling between resorption and formation. It is initiated by activation of osteoclast precursors that become mature osteoclasts by proliferation and differentiation.[8] The osteoclasts cause bone resorption until they have reached a final resorption depth. The osteoblasts then invade the area and begin bone formation. The end product of the remodeling sequence is the bone structural unit which is characterized by a certain structural thickness. The sequence of events in remodelling, i.e. activation – resorption – formation (ARF sequence), is most easily demonstrated in cortical bone.[9] The space corresponding to the amount of bone resorbed by osteoclasts but not formed by osteoblasts is the remodeling space. Activation frequency indicates how often a given site of the bone surface undergoes resorption and subsequent formation. Normal trabecular bone is activated with an interval of 2–3 years, whereas the activation frequency in cortical bone is lower.[9] Besides paracrine and local factors, the activation frequency is regulated by a variety of hormones; PTH, $1,25(OH)_2D$, growth hormone and thyroid hormones increase the activation frequency, and calcitonin, corticosteroid and estrogen reduce the activation frequency.

Bone Mineral Metabolism Homeostasis in Hyperthyroidism

The first report of hyperthyroid bone disease was published in 1891 when von Recklinghausen described the "worm eaten" appearance of long bones of a young woman who died due to hyperthyroidism.[10] Plummer gave similar description in 1920 and reported – "A 53 year old woman gave a history of hyperthyroidism. The patient died three hours after operation. The ribs showed multiple fractures, were very friable and could easily be crushed between the fingers. The calvarium was found to be extremely thin, and was almost translucent when held up to the light". In early part of the century, emphasis of studies in thyrotoxicosis was on calcium–phosphorus metabolism. With the introduction of antithyroid drugs and radioiodine therapy in 1940s, clinically apparent hyperthyroid bone disease became less common. In 1970s, with the availability of serum 25(OH)D assay, there was resurgence of interest in vitamin D metabolism in hyperthyroidism. Recently introduced methods of bone density measurement like dual-energy X-ray absorptiometry (DEXA), as well as biochemical markers of bone resorption and formation, have led to further interest in hyperthyroidism related bone disease.[11] These newer techniques have documented skeletal loss in patients with hyperthyroidism, as well as in those on excessive thyroid hormone replacement.

Histomorphometric studies demonstrate that thyroid hormones increase the activation of new remodeling cycles and stimulate osteoclastic and osteoblastic activity in trabecular and cortical bone. In an *in vitro* organ culture of fetal rat bone, Mundy *et al.* demonstrated a direct stimulation of bone resorption by thyroid hormones.[12] Addition of thyroid hormone increased ^{45}Ca release by 10–60% during a 6-day long culture of bones of fetal rats previously treated with radioisotope. Histologically, an increase in number and activity of osteoclasts was detected. These cells appeared similar to those seen in cultured bone treated with PTH.[12] The stimulation of bone resorption was inhibited by cortisol, calcitonin and phosphate as well as by propranolol. The mechanisms of thyroid hormone induced bone resorption include cAMP-mediated, increased sensitivity of beta adrenergic receptors to catecholamines, increased sensitivity of bone cells to PTH, osteoclast activator factor and interleukin-1 (IL-1) mediated increased bone resorption.[13] Thyroid stimulating hormone (TSH) deficiency, rather than thyroid hormone excess, has been suggested as the underlying cause. To investigate the molecular mechanism of osteoporosis in thyroid disease, Basstt *et al.* characterized the skeleton in mice lacking either thyroid hormone receptor α or β ($TR_\alpha^{0/0}$, $TR\beta^{-/-}$). Remarkably, in the presence of normal circulating thyroid hormone and TSH concentrations, adult $TR_\alpha^{0/0}$ mice had osteosclerosis accompanied by reduced osteoclastic bone resorption, whereas juveniles had delayed endochondral ossification with reduced bone mineral deposition. By contrast, adult $TR\beta^{-/-}$ mice with elevated TSH and thyroid hormone levels were osteoporotic with evidence of increased bone resorption, whereas juveniles had advanced ossification with increased bone mineral deposition. Analysis of T_3 target gene expression revealed skeletal hypothyroidism in $TR_\alpha^{0/0}$ mice, but skeletal thyrotoxicosis in $TR\beta^{-/-}$ mice. These studies demonstrate that bone loss in thyrotoxicosis is independent of circulating TSH levels and mediated predominantly by TR_α. This study suggests TR_α as a novel drug target in the prevention and treatment of osteoporosis.[14]

Alterations in Calcium Homeostasis in Hyperthyroidism

The majority of patients with hyperthyroidism in the West have normal or increased serum total calcium levels and the mean plasma calcium concentration is higher than in

the control subjects. Till 1963, only 31 cases of thyrotoxic hypercalcemia were reported in literature.[13] In 1966, Baxter and Bondy reported hypercalcemia in 19 of the 77 patients (23%) with hyperthyroidism. In another series, percentage of patients with hypercalcemia in thyrotoxic state varied between 5 and 27%.[15] Manicort *et al.* observed an increase in serum free calcium in 50% of subjects with hyperthyroidism.[16] Propranolol therapy also improves hypercalcemia of hyperthyroidism. Hypercalcemia usually resolves after attainment of euthyroid state. Reversibility of hypercalcemia has been observed with all therapeutic modalities, i.e. subtotal thyroid resection, antithyroid drugs and radioiodine therapy. Magnitude of disturbances in serum calcium in hyperthyroidism correlates with serum T3 levels.[5,15] Severe (>15 mg/dl) and symptomatic hypercalcemia is rare among patients with hyperthyroidism. Symptomatic hypercalcemia responds to rehydration, use of corticosteroids, calcitonin and phosphate therapy.

Renal calcium excretion is usually increased in hyperthyroidism and correlates positively with excess thyroid hormone levels and cortical osteoclastic activity. It is caused by enhanced mobilization of bone mineral in hyperthyroid state and remains elevated even on calcium deficient diet. In kidney, the filtered calcium load is enhanced due to increase in serum ultrafiltrable calcium and glomerular filtration rate (GFR) as well as reduced tubular reabsorption because of suppressed PTH levels.

Alteration in Phosphorous Homeostasis in Hyperthyroidism

There are variable reports on serum phosphorous levels in patients with hyperthyroidism. Most of the studies indicate hyperphosphatemic state. However, a few studies show normal or low levels of serum phosphorous.[5] Hyperphosphatemia in hyperthyroidism has been explained on the basis of an enhanced tissue catabolism leading to an excess input of phosphorous to the plasma pool from bone and tissues and lower fractional clearance of phosphorous and increased renal tubular reabsorption of phosphorous.[5] The changes in serum phosphorous are due to suppressed PTH levels as well as direct effects of thyroid hormones on tissue phosphate metabolism and renal phosphate handling. These effects lead to increased filtered load of phosphorous in patients with hyperthyroidism. Antithyroid treatment normalizes serum phosphorous concentration.

Alkaline Phosphatase Levels in Hyperthyroidism

Patients with hyperthyroidism have elevated levels of serum alkaline phosphatase in as many as 50% of cases.[17] A direct correlation between serum thyroxine concentration and serum alkaline phosphatase levels has been found by several workers. The raised levels of serum alkaline phosphatase levels could be either of hepatic or of bone origin. Following treatment, serum alkaline phosphatase levels remain elevated for several months suggesting increased bone turnover continues even after restoration of a normal metabolic rate.

Parathyroid Hormone Secretion in Hyperthyroidism Disease

Bouillon and DeMoor first reported a decrease in serum PTH concentration in patients with hyperthyroidism.[18] The above observation has been confirmed by other investigators as well.[19] However, some researchers could not demonstrate a decline in serum PTH levels among patients with hyperthyroidism, possibly due to difficulty in differentiating between normal and decreased concentrations due to less sensitive PTH assays. There is inverse relationship between serum calcium and serum PTH levels, indicating that increased serum calcium levels inhibit PTH secretion from parathyroid gland. Suppressed PTH levels also explain the raised serum phosphorous and increased maximal tubular absorption rate for phosphorous.

Vitamin D and its Metabolites in Hyperthyroidism

Serum levels of 25(OH)D, 1,25$(OH)_2$D and other metabolites of vitamin D have been studied by various investigators.[20] Most of the studies have documented normal serum levels of 25(OH)D levels in hyperthyroidism.[21,22] However, there are few reports of subnormal 25(OH)D levels in patients with hyperthyroidism.[23] Ventertazs *et al.* and Mosekilde *et al.* reported significantly lower plasma 25(OH)D levels in thyrotoxic patients when compared to the values observed in controls. However, no correlation was observed between serum 25(OH)D and bone histomorphometry. Recently, Yamashita *et al.* have reported subnormal levels of 25(OH) D levels in 40% of females and 18% of males in a series of 208 patients with Graves' disease.[24] The subnormal levels of mean plasma 25(OH)D levels in the above studies was postulated to be due to reduced intestinal absorption of vitamin D due to steatorrhea or hepatic enzyme induction, reduced sun exposure or deficient vitamin D intake in diet.[24] There is only one published study available from India by Dhanwal *et al.*[2] In this study, 30 patients of thyrotoxicosis were studied for vitamin D status and bone mineral density (BMD). Thirty percent patients had severe vitamin D deficiency (<10 ng/ml). In subjects with hyperthyroidism, high serum calcium, low PTH and

high phosphorous levels suppress renal 25(OH)D1-α hydroxylase activity leading to decrease in $1,25(OH)_2D$ levels. Serum $24,25(OH)_2D$ levels are increased in patients with hyperthyroidism and they correlate with serum thyroid hormone levels.[17]

Hyperthyroidism and Bone Density

Hyperthyroidism is an important cause of secondary osteoporosis. Early studies have used conventional radiography to assess bone mineral content.[25] During 1970s–1980s, single photon absorptiometry and dual photon absorptiometry were used to quantify BMD at various sites. Tsai *et al.* studied BMD in 24 untreated patients with hyperthyroidism using dual photon absorptiometry and showed significant increase after 1 year treatment with antithyroid drugs and propranolol.[26] From 1991 onward, dual energy absorptiometry (DEXA) has been available for BMD measurements. DEXA allows rapid, accurate and highly reproducible assessment of mineral content with a minimal exposure to radiation. Bayley *et al.* (1980) studied bone mineral and muscle mass using *in vivo* neutron activation analysis in patients with hyperthyroidism before and after treatment. Reversibility of both bone mineral mass and body muscle mass was recorded after 1 year of treatment with radioiodine therapy.[27]

Krolner *et al.* investigated 25 patients with hyperthyroidism and demonstrated 12.5% lower bone mineral content at lumbar spine when compared to healthy controls. In this study, lumbar bone mineral content increased by 3.7% after 1 year of antithyroid therapy. Most of the subsequent studies have shown significant increase in BMD following treatment.[27,28] Indian situation is also peculiar in that despite adequate sunlight, vitamin D deficiency is prevalent in our country. There are few published studies from India on hyperthyroidism and bone density. Udayakumar and co-workers have reported 32% osteopenia and 60% osteoporosis in a group of 50 hyperthyroid patients. They also demonstrated reversal of bone loss after 1 year treatment with antithyroid medications.[29]

In a recently concluded study, we have found that in contrast to Western data, hypercalcemia is not a feature of Indian patients with hyperthyroidism. In fact, 26% of these patients showed hypocalcemia and 30% of these patients had concomitant vitamin D deficiency.[2] In this study, BMD expressed as T score was in the osteoporotic range in 20%, 36%, and 22% at hip, forearm and lumbar spine, respectively. BMD was compared in vitamin D-deficient and -sufficient patients, and it was observed that vitamin D deficient patients have more severe bone loss. The author has also reported reversibility of bone loss after 1 year of medical therapy at hip and spine but deterioration of bone loss at fore arm.[30]

Thus, Indian patients with thyrotoxicosis are different from the Western patients from bone mineral homeostasis point of view. These patients have hypocalcemia rather then hypercalcemia as seen in the West and this is due to associated vitamin D deficiency. Future scientific work is needed to study the effect of vitamin D in therapeutic doses in patients with hyperthyroidism with concomitant vitamin D deficiency. Our group at Maulana Azad Medical College, New Delhi, is studying the effect of vitamin D supplementation with antithyroid therapy on BMD in hyperthyroidism.[31]

In summary, patients with hyperthyroidism have significant impact on bone mineral homeostasis. Western data suggest that these patients have hypercalcemia, hyperphosphatemia, raised alkaline phosphatase and reduced BMD. However, the available data from India suggest that due to concomitant vitamin D deficiency, these patients have normal calcium levels and increased bone loss.

Hypothyroidism and Bone

The signs and symptoms of hypothyroidism in general are opposite of thyrotoxicosis but this may not be true as far as bone metabolism is concerned. For example, the fracture risk in patients with hypothyroidism is increased as reported by Vestergaard *et al.*[32] In this population-based study, 11,776 patients with hyperthyroidism (6301 patients with diffuse toxic goiter, mean age: 52.1 ± 18.6 years; and 5475 with nodular toxic goiter, mean age: 60.4 ± 15.9 years) and 4473 patients with hypothyroidism (mean age: 66.1 ± 17.3 years) were identified. In patients with hyperthyroidism, fracture risk was only significantly increased around the time of diagnosis [incidence rate ratio (IRR) between 1.26 and 2.29], but decreased to normal levels after diagnosis. Surgical treatment of hyperthyroidism was associated with a decreased fracture risk after diagnosis [RR = 0.66, 95% confidence interval (CI): 0.55–0.78]. In hypothyroidism, fracture risk was significantly increased both before and after diagnosis with a peak around the time of diagnosis (IRR between 2.17 and 2.35). This study concluded that fracture risk is increased in hyperthyroidism and hypothyroidism. Thyroid surgery seems associated with a decreased fracture risk in hyperthyroid patients.

It seems that there is increase in bone density in adult subjects with hypothyroidism, but the bone quality is poor which is responsible for the possible increase in fracture in these patients. In Trosmo study, Grimnes *et al.* have reported that postmenopausal women with serum

TSH above 97.5 percentile had significantly higher BMD at the femoral neck than women with serum TSH in the normal range.[33] However, in children with congenital hypothyroidism, BMD was lower than in the normal children.[34] Bone quality was studied by Nagata *et al.* using quantitative ultrasound (QUS) in subjects with subclinical hypothyroidism. Calcaneo Osteo Sono assessment indices (OSI) of right feet were measured by ultrasound bone densitometer.[35] The results showed that OSI decreased according to the increase in TSH concentration. This suggests that hypothyroidism affects bone structure as assessed by QUS.

Summary

Thyroid hormones play an important role in bone mineral homeostasis and bone density. Both hyperthyroidism and, to some extent, hypothyroidism are associated with reduced BMD leading to increased fracture risk. With changing worldwide geographic occurrence of hip fractures, it is important to keep in mind the impact of thyroid disorders as a secondary cause of osteoporosis.[36,37] Reduced bone density in thyrotoxicosis is reversible with treatment irrespective of the method of treatment. Indian data suggest that majority of Indian patients with hyperthyroidism have concomitant vitamin D deficiency which aggravates bone loss. Further research is needed to study the impact of vitamin D supplementation in these subjects with hyperthyroidism on bone density and fracture risk reduction.

References

1. Dawson-Hughes B, Mithal A, Bonjour JP, Boonen S, Burckhardt P, Fuleihan GE, *et al*. IOF position statement: Vitamin D recommendations for older adults. Osteoporos Int 2010;21:1151-4.
2. Dhanwal DK, Kochupillai N, Gupta N, Cooper C, Dennison EM. Hypovitaminosis D and bone mineral metabolism and bone density in hyperthyroidism. J Clin Densitom 2010;13:462-6.
3. Goswami R, Tandon RK, Dudha A, Kochupillai N. Prevalence and significance of steatorrhea in patients with active Graves' disease. Am J Gastroenterol 1998;93:1122-5.
4. Goswami R, Kochupillai N. Adrenocortical reserve in patients with Graves' disease. Eur J Endocrinol 2001;144:85.
5. Mosekilde L, Christensen MS. Decreased parathyroid function in hyperthyroidism: inter relationship between serum parathyroid hormone, calcium phosphorus metabolism and thyroid function. Acta Endocrinol (Copenh) 1977;84:566-75.
6. Bikle DD. Regulation of bone mineral homeostasis: An integrated new. In: Favus MJ, editor. Primer on the metabolic bone disease and disorders of mineral metabolism. New York: Raven Press; 1993. p. 76-82. 8.
7. Portman AW, Heny HL. Vitamin D: Metabolism and mechanism of action. Primer on the metabolic bone disease and disorders of mineral metabolism. New York: Raven Press; 1993. p. 63-9.
8. Eriksen EF. Normal and pathological remodeling of human trabecular bone. Three-dimensional reconstruction of the remodeling sequence in normal and in metabolic bone disease. Endocr Rev 1986;7: 379-408.
9. Eriksen EF, Melsen F, Mosekilde L. Reconstruction of the resorption site and iliac trabecular bone. A kinetic model for bone resorption in 20 normal individuals. Metab Bone Dis Relat Res 1984;5:235-42.
10. Reimer G. von Rechklinghausen F in Festschrift R, Virchow. Vol 12. Berlin: 1891. p. 20.
11. Wahner HW, Fogelman I. The evaluation of osteoporosis. Dual energy x-ray absoptiometry in clinical practice. London: Martin Dunitz, 1994.
12. Mundy GR, Shapiro JL, Bandelin JG, Canalis EM, Raisz LG. Direct stimulation of bone resorption by thyroid hormones. J Clin Invest 1976;58:529-34.
13. Gowen M, Wood DD, Ihrie EF, McGuire MKB, Russel GG. An inteleukin like factor stimulates bone absorption *in vitro*. Nature 1983;306:378-80.
14. Bassett JH, O'Shea PJ, Sriskantharajah S, Rabier B, Boyde A, Howell PG, *et al*. Thyroid hormone excess rather than thyrotropin deficiency induces osteoporosis in hyperthyroidism. Mol Endocrinol 2007;21:1095-107.
15. Baxter JD, Bondy PK. Hypercalcemia of thyrotoxicosis. Ann Intern Med 1966;65:429-42.
16. Manicourt D, Detester Mirking N, Brauman H, Corvilain J. Disturbed mineral metabolism in hyperthyroidism: Good correlation with tri-iodothyronine. Clin Endocrinol (Oxf) 1979;10:407-12.
17. Mosekilde L, Christensen MS, Melsen F, Sorensen NS. Effect of anti-thyroid treatment on calcium phosphorus metabolism in hyperthyroidism. 1: Chemical quantities in serum and urine. Acta Endocrinol (Copenh) 1978;87:743-50.
18. Bouillon R, DeMoor P. Parathyroid function in patients with hyper or hypothyroidism. J Clin Endocrinol Metab 1974;38:999-1004.
19. Bommer J, Ritz E, Gengenbach E. Parathyroid activity in hyperthyroidism. Calcif Tissue Res 1976;21 Suppl:288-93.
20. Bouillon R, Muls E, DeMoor P. Influence of thyroid function on the serum concentration of 1.25-dihydoryvitamin D3. J Clin Endocrinol Metab 1980;51:793-7.
21. Macfarlane IA, Mawer EB, Berry J, Hann J. Vitamin D metabolism in hyperthyroidism. Clin Endocrinol (Oxf) 1982;17:51-9.
22. Mosekilde L, Lund B, Sorensen OH, Christensen MS, Melsen F. Serum 25- hydroxycholecalciferol in hyperthyroidism. Lancet 1977;1:806-7.
23. Velentzas C, Orepoulos DB, From G, Porret B, Rapopart A. Vitamin D levels in thyrotoxcosis. Lancet 1977;1:370-1.
24. Yamashita H, Nognchi S, Takatsu K, Koike E, Murakami T, Watanabe S, *et al*. High prevalence of vitamin D deficiency in Japanese female patients with Graves' disease. Endocr J 2001;48:63-9.
25. Fraser SA, Anderson JB, Smith DA, Wilson GM. Osteoporosis and fractures risk following thyrotoxicosis. Lancet 1971;1:981-3.
26. Tsai KS, Lai SM, Huang KM, Chieng PU, Su CT, Chen FW. Decreased bone mineral density in patients with prolonged thyrotoxicosis before and after treatment. J Formos Med Assoc 1991;90:250-5 .
27. Bayley TA, Harrison JE, McMeill KG, Mernagh JR. Effect of thyrotoxicosis and its treatment on bone mineral and muscle mass. J Clin Endocrinol Metab 1980;50:916-22.
28. Krolner B, Jorgensen JV, Nielsen SP. Spinal bone mineral content in myxoedema and thyrotoxicosis. Effect of thyroid hormones and antithyroid treatment. Clin Endocrinol (Oxf) 1983;18:439-46.
29. Udayakumar N, Chandrasekaran M, Rasheed MH, Suresh RV, Sivaprakash S. Evaluation of bone mineral density in thyrotoxicosis. Singapore Med J 2006;47:947-50.
30. Dhananwal Dinesh, Dixit V, Marwaha V. Bone mineral homeostasis

and bone mineral densilty in patients with hyperthyroidism after vitamin D therapy. UGC, Major Research Project, India. 2011.

31. Dhanwal D, Gupta N. Bone mineral density trends in Indian patients with hyperthyroidism after medical therapy. J Assoc Physicians India 2011 [In Press].
32. Vestergaard P, Mosekilde L. Fractures in patients with hyperthyroidism and hypothyroidism: A nationwide follow-up study in 16,249 patients. Thyroid 2002;12:411-9.
33. Grimnes G, Emaus N, Joakimsen RM, Figenschau Y, Jorde R. The relationship between serum TSH and bone mineral density in men and postmenopausal women: The Tromsø study. Thyroid 2008;18:1147-55.
34. Demartini Ade A, Kulak CA, Borba VC, Cat MN, Dondoni RS, Sandrini R, *et al*. Bone mineral density of children and adolescents with congenital hypothyroidism. Arq Bras Endocrinol Metabol 2007;51:1084-92.
35. Nagata M, Suzuki A, Sekiguchi S, Ono Y, Nishiwaki-Yasuda K, Itoi T, *et al*. Subclinical hypothyroidism is related to lower heel QUS in postmenopausal women. Endocr J 2007;54:625-30.
36. Dhanwal DK, Dennison EM, Harvey NC, Cooper C. Epidemiology of hip fracture: Worldwide geographic variation. Indian J Orthop 2011;45:15-22.
37. Dhanwal DK, Cooper C, Dennison EM. Geographic variation in osteoporotic hip fracture incidence: the growing importance of Asian influences in coming decades. J Osteoporos 2010;2010:757102.

Cite this article as: Dhanwal DK. Thyroid disorders and bone mineral metabolism. Indian J Endocr Metab 2011;15:S107-12.

Source of Support: Nil, **Conflict of Interest:** None declared.