Int. J. Pure Appl. Sci. Technol., 30(1) (2015), pp. 18-23

International Journal of Pure and Applied Sciences and Technology

ISSN 2229 - 6107

Available online at ***www.ijopaasat.in***

Research Paper

Thyroid Dysfunction - Risk of Fracture

Gulab Kanwar[1], Monika Shekhawat[2,*], Ashwin Gondane[3], Nidhi Sharma[4], Rinki Hada[5] and Chandrajeet Singh Chandel[6]

[1] Professor & Head, Department of Biochemistry, Govt. Medical College, Kota, Rajasthan, India

[2] 2nd Year MD Resident, Department of Biochemistry, Govt. Medical College, Kota, Rajasthan, India

[3] 2nd Year MD Resident, Department of Orthopaedics, Govt. Medical College, Kota, Rajasthan, India

[4] 2nd Year MS Resident, Department of Biochemistry, Govt. Medical College, Kota, Rajasthan, India

[5] Senior Demonstrator & Head, Department of Physiology, Govt. Medical College, Kota, Rajasthan, India

[6] Tutor, Department of Anatomy, R.U.H.S. College of Medical Sciences, Jaipur, Rajasthan, India

* Corresponding author, e-mail: (drmonikashekhawat@gmail.com)

(Received: 2-8-15; Accepted: 29-9-15)

Abstract: *Thyroid diseases are common worldwide. India too carries a significant burden of the same. Thyroid dysfunctions are more commonly seen in females and the incidence increases with age. These mainly affect musculoskeletal system, cardiovascular system and nervous system. Variations in levels of TSH are significantly associated with risk of fracture. The study was conducted in Department of Biochemistry and Orthopaedics, Govt. Medical College, Kota and attached group of hospitals. Duration of study is from September 2014 to May 2015. Level of Thyroid Stimulating Hormone (TSH) was measured. A total of 177 fractured patients of ages between 25 – 50 years of both sexes were included in the study. The estimation of TSH was done by chemiluminescence in Hormonal Assay Lab, Department of Biochemistry, Govt. Medical College, Kota, Rajasthan, India. Among the total 177 fractured patients, we found 8 hyperthyroid (< 0.05mU/L), 12 subclinical hyperthyroid (0.05-0.3mU/L), 5 hypothyroid (>10mU/L), 16 subclinical hypothyroid (4.5-10mU/L) and 136 euthyroid patients (0.3-4.5mU/L). Analysis was done by Microsoft Excel. Mean ± SD of TSH was calculated in all cases. The results were compared by one - way ANOVA between hyperthyroid, subclinical hyperthyroid, hypothyroid, subclinical hypothyroid and euthyroid cases. P value was found to be < 0.05, which is highly significant. Our study shows that the any variations in level of TSH from the normal range, is a risk of fracture.*

Keywords: Fracture, Hyperthyroidism, Hypothyroidism, Subclinical Hyperthyroidism, Subclinical Hypothyroidism, Thyroid Stimulating Hormone (TSH).

Introduction

Thyroid hormones are necessary for normal development and functions of human skeleton. Thyroid dysfunction is highly prevalent, affecting the females more as compared to males (Kumar and Clark, 5th edition). Thyroid hormones affect numerous systems in the human body mainly musculoskeletal, circulatory and nervous system (Boelaert K., 2005). Thyroid Stimulating Hormone (TSH) is a glycoprotein, heterodimer with α subunit of 92 aminoacids and β subunit 112 aminoacids which acts on the thyroid gland by stimulating the synthesis and secretion thyroid hormones (Burtis and Bruns, 7th edition). Thyroid dysfunction is associated with a broad range of metabolic disturbances and conditions such as: osteoporosis, hypercholestremia, obesity and cardiovascular diseases (-Eriksen EF, 1986, Tagami T et al ., 2011 and Rotondi M, 2011). The main patterns of thyroid dysfunctions are hyperthyroidism, subclinical hyperthyroidism, hypothyroidism and subclinical hypothyroidism (Burtis and Bruns, 7th edition). Apart from thyroid follicular cells, the receptors for TSH are located in osteoblasts and osteoclasts (Nicholls J et al., 2012 and Gorka J et al., 2013). Study by Abe et al suggests that TSH is a negative regulator of skeletal remodelling by reducing both differentiation of osteoblasts and formation of osteoclasts (Abe E et al., 2003).

Hyperthyroidism is the increased activity of thyroid gland, common in ages of 20 – 40 years and prevalent in 2-5% population worldwide (Kumar and Clark , 5th edition). It leads to acceleration of bone turnover with restoration of bone exceeding accretion and loss of mineral density, mainly in cortical bone (Basset J et al., 2003, Harvey C et al., 2002, Stevens D et al., 2003 and Burtis and Bruns, 7th edition). Human interest about influence of thyroid hormone on skeleton lasts since a long time. Von Recklinghausen described a correlation between numerous fractures and state of hyperthyroidism over 120 years ago (Nicholls J et al., 2003).

Subclinical hyperthyroidism is the condition in which TSH levels are suppressed whereas FT4 and FT3 are normal (Burtis and Bruns, 7th edition). It is associated with increased risk of fracture (Waring AC et al., 2013 and Wejda B et al., 1995).

Hypothyroidism is decreased activity of thyroid gland. Rate of bone turnover is reduced in hypothyroidism leading to reduction in the pool of exchangeable calcium (Marshall and Bangert, 2nd edition) which impairs bone formation and mineralization (Eriksen EF et al., 1986). Hypothyroidism has been associated with an increased risk of fractures (Ahmed LA et al., 2006 and Vestergaard P et al., 2002) and a risk factor for falls (S.T. Marshall: B.D. Browner, 2012).

Subclinical hypothyroidism is defined as elevation of TSH whereas FT4 levels are seen within the normal range (Fatourechi V et al., 2009). A study by Polovina et al. Suggested that there is a greater risk of fracture seen in subclinical hypothyroidism (Polovina S et al., 2013).

Fracture of bone is a medical condition in which there is a break in continuity of the bone, which may occur as a result of high force impact or stress or trauma. Cortical bone fractures are more common in thyroid dysfunction (S.T. Marshall: B.D. Browner, 2012).

Measurement of plasma TSH concentration provides the cornerstone of biochemical evaluation of thyroid status, both in overt and subclinical primary thyroid disorders (Marshall and Bangert, 2nd edition and Burtis and Bruns, 7thedition). A normal TSH effectively excludes primary thyroid dysfunction. Normal level of TSH is 0.3 – 3.5 mU/L, in hyperthyroidism TSH level is <0.1mU/L and in hypothyroidism, level of TSH > 10mU/L (Burtis and Bruns, 7th edition).

Aim and Objectives

To find out the levels of TSH in males and females having fracture, aged between 25–50 years and so as to establish a relation between thyroid dysfunction of different thyroid categories and risk of fracture. This study may be helpful for public health and clinical practice.

Material and Methods

A total of 177 patients having fracture of ages between 25–50 years of both sexes are included in the study. The patients with chronic renal failure, parathyroid or calcium related diseases, history of therapy with glucocorticoids, calcium & vitamin D, males and females of age <25 years, >50 years and patients on treatment for any thyroid dysfunction were excluded from the study.

Sample: The sample of fractured males and females were collected after confirmation of fracture radio logically. After obtaining consent of the patient, 2ml of blood was withdrawn. Then centrifugation is done, subsequently serum sample obtained was analysed on Roche cobas e 411 by chemiluminescence in Hormonal Assay Lab in Department of Biochemistry, Govt. Medical College, Kota under the state of Rajasthan, India.

Statistical Analysis

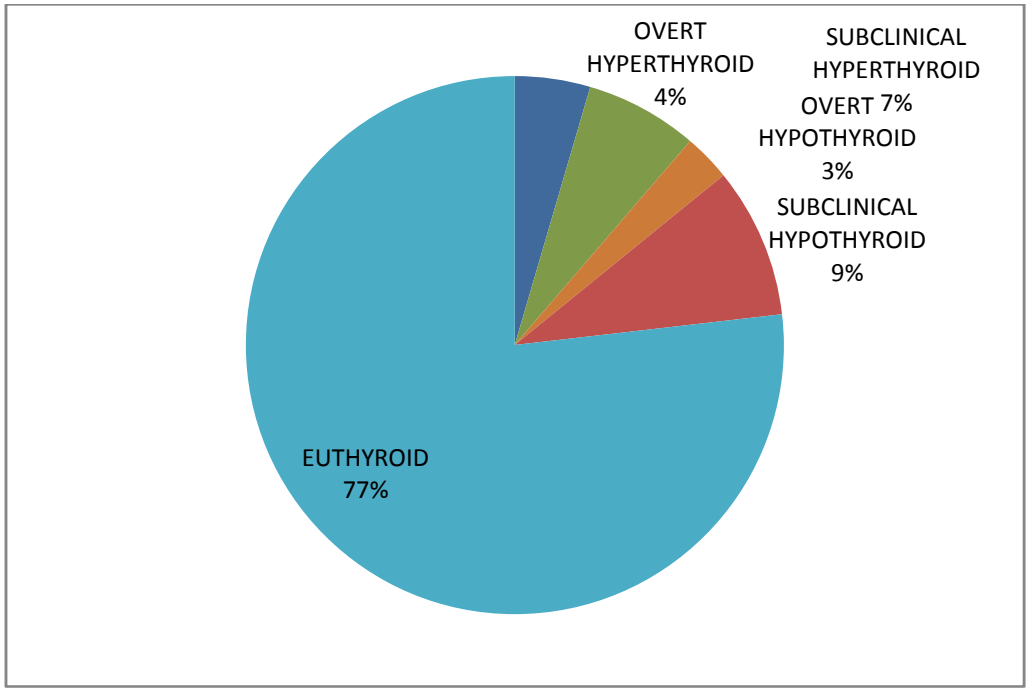
The statistical analysis was performed by using Microsoft Excel Program. The results were expressed as mean ± standard deviation. The P value was calculated and found < 0.05, which was considered statistically significant. The results were compared by one - way ANOVA between hyperthyroid, subclinical hyperthyroid, hypothyroid, subclinical hypothyroid and euthyroid cases.

Results

Among the total 177 fractured patients, we found 8 overt hyperthyroid (< 0.05mU/L), 12 subclinical hyperthyroid (0.05-0.3mU/L), 5 overt hypothyroid (>10mU/L), 16 subclinical hypothyroid (4.5-10mU/L) and 136 euthyroid patients (0.3-4.5mU/L).

Table 1: Showing number of patients in different thyroid categories

S. No.	Type of Thyroid Categories	Number of Patients
1.	Overt Hyperthyroid	8
2.	Subclinical hyperthyroid	12
3.	Overt Hypothyroid	5
4.	Subclinical hypothyroid	16
5.	Euthyroid	136
Total Number of Patients		**177**



Distribution of Patients in Different Thyroid Categories

The mean ± SD in case of hyperthyroidism is 0.027 ± 0.01. The mean ± SD in case of subclinical hyperthyroidism is 0.15 ± 0.03. The mean ± SD in hypothyroidism is 20.1± 2.88. The mean ± SD in case of subclinical hypothyroidism is 6.60 ± 0.88 and the mean ± SD in case of euthyroidism is 2.44 ± 0.94. P value is < 0.05, which is significant.

Table 2: Showing Mean ± SD in different thyroid categories

Parameter	**Overt Hyperthyroid**	**Subclinical hyperthyroid**	**Overt Hypothyroid**	**Subclinical hypothyroid**	**Euthyroid**	**P Value**
TSH(mU/L) Mean ± SD	0.027± 0.01	0.15 ± 0.03	20.1± 2.88	6.60 ± 0.88	2.44 ± 0.94	<0.05*****

***** P value is <0.05, which is significant

Discussion and Conclusion

Thyroid disorders are one of the most common causes of morbidity in the world and India. The effects of thyroid dysfunctions are well documented in all age groups. Thyroid hormones play an important role in integrity and proper formation of skeletal system. TSH exerts a direct effect on bone metabolism independently of peripheral thyroid hormones (T4 and T3), through G –protein coupled trans membrane receptors, which are expressed on osteoblast and osteoclast precursors.

Subclinical hyperthyroidism and hypothyroidism are common clinical entities that encompass mild degree of thyroid dysfunction. These conditions might or might not always constitute an early stage of "overt" thyroid disease.

Thyroid dysfunctions can influence fracture risk both by increased risk of fall (in case of hypothyroidism) (Barrett- Connor E et al., 2009) and a risk for osteopenia and osteoporosis (as seen in hyperthyroidism) (El Hadidy et al.2011 and Udayakumar N et al., 2006). A study by Vestergaard et al. also suggested that hyperthyroidism and hypothyroidism is a risk factor for the occurrence of

fracture (Vestergaard P et al., 2002). In both clinical and subclinical hyperthyroidism, elevation of bone turnover and decreased Bone Mineral Density (BMD) is reported (Kumeda Y et al., 2000). In a population based study by Bauer et al, an association of subclinical hyperthyroidism with increased fracture risk is seen (Bauer DC et al., 2001). Hypothyroidism further reduces osteoblastic bone differentiation, resulting in decrease bone formation and resorption (Coindre JM et al., 1986). Myalgia and arthralgia leads to increase risk of fall thus leading to increased incidence of fracture. Subclinical hypothyroidism is a relatively frequent condition. Bone quality was studied by Nagata et al. using quantitative ultrasound in postmenopausal women with subclinical hypothyroidism and suggested that hypothyroidism affects bone structure (Nagata M et al., 2007).

By this study we conclude that subclinical hyperthyroidism and hypothyroidism is more prevalent than overt hyperthyroidism and hypothyroidism and any variations in level of TSH from the normal range, is a risk of fracture. So, estimation of TSH can be included in routine investigations so that it can decrease the bony pathologies associated with thyroid dysfunction to a great extent, thus it will be helpful by decreasing the morbidity & reduce the DALY (Disability Adjusted Life Years).

Limitations of the Study

1) There is a need to explore this study further.
2) TPO antibodies could not be measured due to certain limitations.
3) Thyroid scan was not done due to limitations.

Acknowledgement

- Department of Biochemistry, GMC, Kota for their kind cooperation.
- Department of Orthopaedics, GMC, Kota for helping us to conduct the study.

References

[1] P. Kumar and M. Clark, Endocrine Disease – Thyroid Dysfunctions: Essentials of Clinical Medicine (5th Edition), Elsevier Publication, (2011), 619-629.
[2] K. Boelaert and J.A. Franklyn, Thyroid hormone in health and disease, *Journal of Endocrinology*, 187(2005), 1-15.
[3] C.A. Burtis and D.E. Bruns, Hormones: Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics (7th Edition), 432(2014), 818-819.
[4] E.F. Eriksen, Normal and pathological remodelling of human trabecular bone: Three dimensional reconstruction of the remodelling sequence in normals and metabolic bone disease, *Endocr Rev.*, 7(4) (1986), 379-408 (PubMed: 3536460).
[5] T. Tagami, H. Kimura and S. Ohtani et al., Multi centre study on the prevalence of hypothyroidism in patients with hypercholesterolemia, 58(6) (2011), 449-457.
[6] M. Rotondi, F. Magri and L. Chiovato, Thyroid and obesity: Not a one way – interaction, *J Clin Endocrinol Metab.*, 96(2) (2011), 344-346.
[7] C.A. Burtis and D.E. Bruns, Hormones: Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics (7th Edition), (2014), 806-823.
[8] J. Nicholls, M. Brassil, G. Williams and J. Basset, The skeletal consequence of thyrotoxicosis, *J Endocrinol*, 213(2012), 209-211.
[9] J. Gorka, R.T. Gjevre and T. Arnason, Metabolic and clinical consequences of hyperthyroidism on bone density, *Int J Endocrinol*, Article ID 638727(2013), 1-11.
[10] E. Abe, R.C. Marians, W. Yu, T. Ando, Y. Li, J. Iqbal, L. Eldeiry, G. Rajendren, H.C. Blair, T.F. Davis and M. Zaidi, TSH is a negative regulator of skeletal remodelling, *Cell*, 115(2003), 151-162.
[11] J. Basset and G. Williams, The molecular actions of thyroid hormone in bone, *Trends Endocrinol Metab*, 14(2003), 356-364.

[12] C. Harvey, P. O'Shea, A. Scott, H. Robson, T. Siebler, S. Shalet, J. Samarut, O. Chassande and G. Williams, Molecular mechanisms of thyroid hormone effects on bone growth and function, *Mol Genet Metab*, 75(2002), 17-30.

[13] D. Stevens, C. Harvey, A. Scott, A. Williams, D. Jackson, P. O'Shea and G. Williams, Thyroid hormone activates fibroblast growth factor receptor-1 in bone, *Mol Endocrinol*, 17(2003), 1751-1766.

[14] C.A. Burtis and D.E. Bruns, Hormones: Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics (7th Edition), (2014), 401-409.

[15] A.C. Waring, S. Harrison, H.A. Fink, M.H. Samuels, P.M. Cawthon, J.M. Zmuda, E.S. Orwoll and D.C. Bauer, A prospective study of thyroid dysfunction, bone loss and fractures in older women: The MrOS study, *Journal of Bone and Mineral Research*, 28(2013), 472-479.

[16] B. Wejda, G. Hintze, B. Katschinski, T. Olbricht and G. Benker, Hip fractures and the thyroid: A case control study, *Journal of Internal Medicine*, 237(1995), 241-247.

[17] W.J. Marshall and S.K. Bangert, Thyroid Dysfunction: Clinical Biochemistry – Metabolic and Clinical Aspects (2nd Edition), (2008), 405-406.

[18] E.F. Eriksen, L. Mosekilde and F. Melsen, Kinetics of trabecular bone resorption and formation in hypothyroidism: Evidence for a positive balance per remodelling cycle, *Bone*, 7(1986), 101-108.

[19] L.A. Ahmed, H. Schirmer, G.K. Bernstsen, V. Fønnebø and R.M. Joakimsen, Self reported diseases and the risk of non – vertebral fractures: The tromsø study, *Osteoporos Int.*, 17(1) (2006), 46-53.

[20] P. Vestergaard and L. Mosekilde, Fractures in patients with hypothyroidism and hyperthyroidism: A nationwide follow up study in 16249 patients, *Thyroid*, 12(5) (2002), 411-19.

[21] E.C. Barrett, T.W. Weiss, C.A. McHorney, P.D. Miller and E.S. Siris, Predictors of falls among postmenopausal women: Results from the national osteoporosis risk assessment (NORA), *Osteoporosis International*, 20(2009), 715-722.

[22] V. Fatourechi, Subclinical hypothyroidism: An update for primary care physicians, *Mayoclin Proc*, 64(2009), 65-71.

[23] S. Polovina, V. Popovic, L. Duntas, N. Milic and D. Micic, FRAX score calculations in postmenopausal women with subclinical hypothyroidism, *Hormones*, 12(2013), 439-438.

[24] S.T. Marshall and B.D. Browner, Chapter 20: Emergency care of musculoskeletal injuries, In: C.M.T. Jr. Sabiston, Textbook of Surgery: The Biological Basis of Modern Surgical Practice (1st Pub. 1956), Elsevier, (2012), 480-520.

[25] W.J. Marshall and S.K. Bangert, Thyroid Dysfunction: Clinical Biochemistry – Metabolic and Clinical Aspects (Second Edition), (2008), 416.

[26] C.A. Burtis and D.E. Bruns, Hormones: Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics (7th Edition), (2014), 402-3.

[27] C.A. Burtis and D.E. Bruns, Hormones: Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics (7th Edition), (2014), 404-6.

[28] H.M. El Hadidy, M. Ghonaim, S.S. El Gawad and M.A. El Atta, Impact of severity, duration and etiology of hyperthyroidism on bone turnover markers and bone mineral density in men, *BMC Endocrine Disorders*, (2011), 11-15, http://www.biomedcentral.com/1472-6823/11/15.

[29] N. Udayakumar, M. Chandrasekaran, M.H. Rasheed, R.V. Suresh and S. Sivaprakash, Evaluation of bone density in thyrotoxicosis, *Singapore Medical Journal*, 47(2006), 947-950.

[30] Y. Kumeda, M. Inaba and H. Tahara et al., Persistent increase in bone turnover in Graves' patients with subclinical hyperthyroidism, *J Clin Endocrinol Metab*, 85(41) (2000), 57-61.

[31] D.C. Bauer, B. Ettinger and M.C. Nevitt et al., Risk for fracture in women with low serum levels of TSH, *Ann Intern Med*, 134(2001), 561-568.

[32] J.M. Coindre, J.P. David, L. Riviere, J.F. Goussot, P. Roger, A. de Mascarel and P.J. Meunier, Bone loss in hypothyroidism with hormone replacement: A histomorphometric study, *Arch Intern Med*, 146(1986), 48-53.

[33] M. Nagata, A. Suzuki, S. Sekiguchi, Y. Ono, K.Y. Nishiwaki and T. Itoi et al., Subclinical hypothyroidism is related to lower heel QUS in postmenopausal women, *Endocr J*, 54(2007), 625-30.