ALKALINE PHOSPHATASE STATUS IN THYROTOXIC INDIVIDUALS

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ABSTRACT

Objectives: To investigate the effect of thyroid hormones, free tri-iodothyronine (T_3) and free tetra-iodothyronine (T_4), on serum alkaline phosphatase in thyrotoxic individuals of Khyber Pakhtunkhwa.

Methods: This comparative cross sectional study had 50 thyrotoxic individuals and 50 controls. Demographic and clinical data of the study individuals was recorded by interviewing and examining them. Blood samples were analyzed for serum FT_3, T_4, and TSH concentration at RIA laboratory, Institute of Radiotherapy and Nuclear Medicine (IRNUM). Serum ALP was determined in Hitech laboratory, Aman Hospital Peshawar respectively. The data was analyzed on SPSS version 13.0 using student t- test.

RESULTS: There was a significant difference between the two groups regarding serum ALP with a P – value of < 0.001

Conclusion: A high concentration of ALP was found in thyrotoxic patients of Khyber Pakhtunkhwa.

Keywords: Free T_3, serum ALP, thyrotoxic, freeT_4, and TSH

INTRODUCTION

The enzymes alkaline phosphatases (ALPs) are a group of enzymes that hydrolyze organic phosphates. It is found in most tissues like the osteoblasts of bone, bile, canaliculi of liver, epithelium of small intestine, proximal tubules of kidneys, placenta, and breast during lactation [1; 47]. Excess of thyroid hormones is associated with increased bone turnover [2; 59]. Elevated serum ALP levels occur in high bone turnover conditions [3; 60].

The optimum pH for alkaline phosphatase is 9, indicating the alkaline environment of bone [4,5; 48, 54]. Total alkaline phosphatase activities more than normal reference range has been noted in serum of hyperthyroid patients. Boomer et al. and Cooper et al. noted increased concentration of ALP in 50% of the hyperthyroid patients [6,7; 55, 56]. Rhone et al. found raised serum ALP activity in 77% of hyperthyroid patients [8;57]. Tibi et al. have shown an increase in total ALP activity in 51% of hyperthyroid patients [9; 58]. However, Cooper et al. did not find a simultaneous increase in 5'-neocleotidase which shows that the increase in serum ALP is due to an elevated osteoblastic activity. After treatment of hyperthyroidism, the serum ALP concentration remains high for several months showing that increased bone turnover continues even after the achievement of euthyroidism and normal metabolic rate [10; 30].

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MATERIALS AND METHODS

Clinically thyrotoxic individuals of any age and either sex belonging to different part of Khyber Pakhtunkhwa (n = 100), referred to Radioimmunoassay (RIA) laboratory for thyroid function tests (TFTs) were enrolled for this cross sectional study and divided on the basis of results of Thyroid Function Tests (TFTs) into thyrotoxic (group I) and euthyroid (group II).

Clinically hyperthyroid patients of any age and either sex visiting/referred to RIA Lab IRNUM hospital for thyroid functions tests were included in this study. Patients with concomitant primary hyper-parathyroidism, malignancy, and hypervitaminosis D were excluded. Data was collected on a Proforma composed of questions (history), physical examination and laboratory tests. A blood sample of approximately 5 ml was drawn from antecubital vein of every subject with disposable syringe using all the aseptic techniques, immediately centrifuged (IEC Model DPR – 6000 centrifuge) at the rate of 1500 – 2000 rpm for 10 minutes and then stored in freezer at – 20 ^{0}C till analysis. The samples were analyzed for serum FT_3 concentration in RIA laboratory at the Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar. Serum concentration of the hormone was determined by Radio Immuno Assay (RIA) method. Serum concentration of ALP was determined by Kinetic colorimetry in Hitech laboratory, Aman Hospital Peshawar.

RESULTS

The normal range of serum ALP is 65 – 270 IU/L. The mean values for serum ALP in our study were

240.26±10.11 IU/L in group of cases and 163.88+4.89 IU/L in the group of controls. There was a significant difference between the two groups regarding serum ALP with a P – value of < 0.001 (Table 1). The maximum and minimum values for cases were 414 IU/L and 74 IU/L respectively, while for controls these were found to be 243 IU/L and 102 IU/L respectively.

DISCUSSION

In this study ALP was increased in cases. Archer, F. J. and Taylor, S. M. have reported elevated concentration of serum ALP in hyperthyroid cats [11; 82].

The increase in ALP is due to the effects of T_4 and T_3 on bone cells i.e. osteoblasts and osteoblast precursors [12; 83]. At higher concentration, Allain et al. have observed T_3 to inhibit cell division and increase the production of ALP and osteocalcin coupled with formation of bone matrix in precursors of osteoblasts as well as primary culture of osteoblasts in experiments on rats [13; 84]. Kumeda et al. have reported a significantly increased serum bone ALP (B-ALP) in Grave's patients with subclinical hyperthyroidism having low TSH as compared to those having normal TSH [14; 85]. Dhanwal D.K. in his literature review has reported elevated levels of ALP in nearly 50% cases; serum ALP concentration remains high for several months after treatment which suggests that the increased bone turnover sustains even though the metabolic rate has become normal [15; 86]. Jyotsna et al. have also noted significantly high ALP in thyrotoxic patients as compared to control. ALP was found raised in 61.25% patients and 15% controls [16; 87].

CONCLUSION

A differential diagnosis of hyperthyroidism should be in mind of a physician in patients with increased concentrations of serum ALP especially those with concomitant bone pains.

REFERENCES

1. Gandapur ASK, Tayyab M. Clinical Chemistry Principles, methods & interpretations; Tahir instruments limited: Lahore Pakistan, 2004; pp 119-125.
2. Archer FJ, Taylor SM. Alkaline phosphatase have isoenzyme and osteocalcin in the serum of hyperthyroid cats. Can. Vet. J. 1996; 37: 735-739.
3. Boelaert K, Franklyn JA. Thyroid hormones in health and disease. J. Endocrin. 2005; 187: 1-15.
4. Shipley M, Rahman A, Graidaigh DO, Compston JE. In Clinical Medicine; Kumar PJ, Clark ML. Eds; Elsevier Limited: Spain, 2009; pp 499-570.
5. Crook,MA. Clinical Chemistry & Metabolic Medicine; Hoddler Arnold: London, 2006; pp 97-104.
6. Swanson TA, Kim SI, Glucksman MJ. Biochemistry and Molecular Biology; Board Review Series; Lippincott Williams & Wilkins: Philadelphia, USA, 2007; pp 44-47.
7. Boomer J, Ritz E, Gengenbach E. Paarathyroid activity in hyperthyroidism. Calcif. Tissue Res. 1976; 21: 288-293.
8. Cooper DS, Kaplan MM, Ridgway EC, Maloof F, Danials GH. Alkaline phosphatase isoenzyme patterns in hyperthyroidism. Ann. Intern. Med. 1979; 90: 164-168.
9. Rhone DP, Berlinger FG, White FM. Tissue sources of elevated serum alkaline phosphatase activity in hyperthyroid patients. Am.J. Clin. Pathol. 1980; 74: 381-386.
10. Tibi L, Patrick AW, Leslle P, Toft AD, Smith AF. Alkaline phasphatase isoenzymes in plasma in hyperthyroidism. Clin. Chem. 1989; 35: 1427-1430.
11. Seeman E, Wahner HW, Offord KP. Differential effects of endocrine dysfunction on the axial and the appendicular skeleton. J. Clin. Invest. 1982; 69: 1302-1309.
12. Fretzl-Zelman N, Horander H, Leugmayr E, Vaiga F, Ellinger A, Erlee MPM, Klaushofer K. Effects of triiodothyronine on morphology of cells and matrix, the localization of alkaline phosphatase, and the frequency of apoptosis in long-term cultures of M C3 T3 - E1 cells. Bone 1997; 20: 225-236.
13. Allain TJ, Thomas MR, McGregor AM, Salisbury JR. A histomorphometric study of bone changes in thyroid dysfunction in rats. Bone 1995; 16: 505-509.
14. Kumeda Y, Inaba M, Taher H, Kurioka Y, Ishikawa T, Mori H, Nishizawa Y. Persistent increase in bone

Table 1: Comparison of serum biochemical parameters between cases and controls

Variables	Groups				t-ratio	P- value
	Cases		Control			
	Mean	SE	Mean	SE		
FT3 (pmol/L)	25.10	1.93	4.53	0.11	10.624	0.001
FT4 (pmol/L)	57.27	2.33	17.98	0.37	16.162	0.001
TSH (m IU/L)	0.03	0.004	1.31	0.12	-10.695	0.001
ALP (IU/L)	240.26	10.11	163.88	4.89	6.801	0.001

turnover in Grave's disease with subclinical hyperthyroidism. J. Clin. Endocrin. Metab. 2000; 85: 4157-4161.

15. Dhanwal DK. Thyroid disorders and bone mineral metabolism. Indian J. Endocrinol. Metab. 2011; 15: S107-112.

16. Jyotsna VP, Sahoo A, Singh AK, Sreenivas V, Gupta N. Bone mineral density in patients of Graves disease pre- & post-treatment in a predominantly vitamin D deficient population. Indian J. Med. Res. 2012; 135: 36-41.