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RESEARCH ARTICLE

VITAMIN C STATUS IN BENIGN HYPOTHYROID NODULES: AN ASSOCIATION STUDY

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ABSTRACT

The thyroid gland constitutes such an organ in our body where oxidative processes are indispensible for the biosynthesis of thyroid hormones. Hydrogen peroxide and free radicals produced from iodine and tyrosine residues participate in various metabolic processes in the thyroid. This makes oxidative stress common in thyroid disorders. Vitamin C is one of the most important nutritional antioxidant and free radical scavengers present in our body. The purpose of this study is to evaluate vitamin C levels in hypothyroid patients with benign thyroid nodules and correlate them with thyroid function and disease status.

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INTRODUCTION

Thyroid nodules are discrete structures within the thyroid gland which are different from the surrounding tissue. They may be toxic or non-toxic. Out of these non-toxic ones have greater potential of turning malignant. Apart from cases of iodine deficiency they are most commonly associated with fluctuating thyroid hormone levels resulting in the formation of nodules. Oxidative stress is defined as a misbalance between the concentration of reactive oxygen species (ROS) and antioxidants in our body. These molecules (ROS) are free radicals that participate in a variety of metabolic processes. A rise in the concentration of such species is known to take part in the pathogenesis of various diseases including cancer (Bankson *et al*., 1993). Oxidative processes are necessary and take place in all organs; however they are indispensible in the thyroid gland due to their role in thyroid hormone synthesis. Large amounts of hydrogen peroxide and free radicals are produced in the thyroid gland during thyroid hormone biosynthesis. Thus oxidative stress is common in thyroid tissues which might also have an active role in proliferation of thyroid tumours (Yanagawa *et al*., 1999; Fujita, 2002). The antioxidant system of our body consists of antioxidant enzymes and small molecule antioxidants (Bray, 1999). Vitamin C is the primary water-soluble, non-enzymatic antioxidant in plasma and tissues (Combs and Gerald, 2012; Erdman *et al*., 2012). Even in small amounts vitamin C can protect important molecules in the body, such as proteins, lipids, carbohydrates, and nucleic acids, from damage by free radicals and reactive oxygen species (ROS). The main role of vitamin C in the thyroid is as a cellular antioxidant protecting the cells against oxidative damage, however earlier studies have also shown the effect of vitamin C on the sodium iodide symporter and iodine uptake (Guy E. Abraham, David Brownstein, 2005). The main objective of this study is to evaluate the level of vitamin C in hypothyroid patients with nodular goitre and to investigate it's relation with disease status.

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MATERIALS AND METHODS

Total 30 cases having hypothyroidism with benign thyroid nodules and 10 control cases were screened from the outpatient department of Ramakrishna Mission Seva Pratishthan. The study was approved by the institutional ethics committee. Blood was collected after obtaining informed consent from each patient. Diagnosis was confirmed by biochemical, radiology and pathological tests. The nodules were classified into Colloid nodules, Adenomatous or Hyperplastic nodules and Nodules in autoimmune thyroiditis (without toxic features). The age and sex of patients and control were matched. The controls were free from any systemic diseases.

Blood samples (fasting) were collected by venous arm puncture into EDTA vacutainers. Plasma was separated for analysis of Vitamin C. Estimation of Vitamin C levels was done by the method of Omaye *et al*. (1979). The dehydroascorbic acid formed due to oxidation of ascorbic acid by copper forms a coloured product on treatment with 2,4-dinitrophenyl hydrazine which was measured at an absorbance of 520nm. A standard curve was prepared using freshly prepared solution containing 0.5mg/dl, 1.0 mg/dl, 1.5 mg/dl, 2.0 mg/dl and 2.5 mg/dl of ascorbic acid. The values obtained were expressed as mean±SD.

conditions. In 2008, a study revealed an increased generation of ROS and impairment of the antioxidant system in patients with hyperthyroidism and particularly in patients with hypothyroidism (Erdamar *et al*., 2008). It indicated that thyroid hormones have a strong impact on oxidative stress and the antioxidant system. Earlier studies had shown low levels of Vitamin C in hyperthyroidism (Dubey *et al*., 1977; Alicigüzel *et al*., 2001) however studies associating vitamin C status and non-toxic nodular thyroid diseases are rare. A large experimental study reported that all subjects with benign or malignant thyroid disease had low levels of antioxidants,

Table 1. Number, Age and sex of study group and control group

	STUDY GROUP			CONTROL GROUP		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
NUMBER	5	25	30	3	7	10
AGE (yrs)	40±15 (min-18 Max-60)	39±11 (min-20 Max-59)	-	44±15 (min-30 Max-60)	41±13 (min-22 Max-56)	-

Table 2. General biochemical parameters of study group and control group

PARAMETERS	VALUES (Mean±SD)		Reference Range
	Study Group	Control Group	
Serum TSH	8.55±4.319 uIUml^{-1}	2.68±0.824 uIUml^{-1}	0.27-4.2 uIUml^{-1}
Serum T3(TOTAL)	1.26±0.209 ng ml^{-1}	1.60±0.408 ng ml^{-1}	0.9-2.0 ng ml^{-1}
Serum T4(FREE)	0.854±0.270 ng ml^{-1}	0.854±0.270 ml^{-1}	0.8-1.8 ml^{-1}
Anti TPO antibody	Patients with autoimmune thyroiditis had values higher than 5.69IU/ml.	None had values higher than 5.69IU/ml	< 5.69 IU ml^{-1}

Table 3. Vitamin C levels in different types of hypothyroid nodules

Study Group (Classification according to cytopathological nature of nodules)	Vitamin C levels (Mean ± SD)
Colloid nodules	0.85±0.39 mgdl^{-1}
Adenomatous or hyperplastic nodules	0.82±0.28 mgdl^{-1}
Nodules in autoimmune thyroiditis (without toxic features)	0.72±0.26 mgdl^{-1}
Control group	1.26±0.36 mgdl^{-1}

RESULTS

Table 1 shows the number, age and sex of all the cases. Out of the 30 patients, 25 were female and 5 were male indicating that hypothyroidism and subsequently development of nodules is more common in female subjects than in male. Table 2 shows the general biochemical parameters of thyroid physiology which confirmed the diagnosis of hypothyroidism and autoimmune thyroiditis. Final classification of the nature of the nodules was done with the help of ultrasonography and fine needle aspiration cytology. Table 3 illustrates the values of vitamin C levels estimated in comparison to healthy controls. In all the types of cases Vitamin C levels were found to be lower than that in case of healthy controls. The percentage of patients with Vitamin C levels below threshold concentration was approximately 16%. In general, vitamin C levels in patients with nodules in autoimmune thyroiditis were found to be lower than that in case of adenomatous nodules or colloid nodules.

DISCUSSION

Vitamin C is a very important antioxidant in plasma and scavenges a variety of oxidants. It has an important role in inflammatory and anti-oxidative processes of the body (Moncayo and Moncayo, 2007; Fang *et al*., 2002). Numerous studies have confirmed the presence of excess oxidative stress and a deteriorated antioxidant defense system in thyroid particularly selenium, zinc, and vitamin C (Roy Moncayo *et al*., 2008). Recently a study by Ramirez *et al*. demonstrated the effects of vitamin C on the absorption of a synthetic T4 hormone with 31 patients who either had autoimmune thyroiditis or idiopathic hypothyroidism. Prior to the study, all patients were not in good control when taking the synthetic T4. Serum concentrations of T3, T4, and TSH were measured at particular intervals after vitamin C therapy. All three concentrations were improved while taking vitamin C (Jubiz and Ramirez, 2014). These findings are significant in evaluating the role of vitamin C in thyroid diseases.

Conclusion

Our present study focuses to associate the levels of Vitamin C with benign nodular goiters in hypothyroidism. Results of our work shows lower levels of vitamin C in all three types of nodular goiters included in the study. Further research is required in this field which might shed light on important physiological and biochemical changes in the thyroid gland in a state of increased oxidative stress.

However based on current findings it can be summed up that Vitamin C deficiency in hypothyroid subjects with benign thyroid nodules may indicate the presence of enhanced oxidative stress which is an inevitable consequence of the metabolic processes involved in the pathogenesis of benign nodular non-toxic thyroid disease.

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Conflicts of interest

None declared.

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