Original Article

Serum Thyroglobulin—A Sensitive Biomarker of Iodine Nutrition Status and Affected by Thyroid Abnormalities and Disease in Adult Populations*

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Abstract

Objective To evaluate the usefulness of the thyroglobulin (Tg) level in adults as a nutritional biomarker of iodine status and to identify the factors related to the serum Tg level.

Methods A cross-sectional study was conducted in adult populations of areas differing in iodine nutrition from three provinces (Autonomous Region) in China. Serum levels of thyroid hormones and Tg as well as thyroid autoantibodies were measured. The thyroid volume and nodule were measured by ultrasound. A multivariate linear regression analysis was used to assess iodine intake and other indeterminate factors associated with the serum Tg level.

Results A total of 573 adults were recruited for this study. The serum Tg levels differed significantly among the three groups (22.27 μg/L, 9.73 μg/L and 15.77 μg/L in the excess, more-than-adequate, and deficient groups, respectively). The results of multivariate linear regression analysis indicate that excess and deficient iodine intake, goiter, thyroid nodule, hypothyroidism are significantly related with higher Tg level, and TgAb positivity is significantly related with lower serum Tg.

Conclusion The serum Tg level reflects abnormal thyroid function and is a sensitive functional biomarker of iodine nutrition status.

Key words: High iodine; Iodine deficiency; Thyroglobulin

Biomed Environ Sci, 2017; 30(7): 508-516 *doi: 10.3967/bes2017.067* *ISSN: 0895-3988*

www.besjournal.com (full text) *CN: 11-2816/Q*

INTRODUCTION

Iodine is an essential trace element used by the thyroid gland to produce thyroid hormones required for normal growth and development[1]. Both iodine deficiency and excess intake may lead to thyroid dysfunction or disease. Iodine deficiency has widespread implications, which include cretinism, endemic goiter, intellectual impairments, increased pregnancy loss and infant

*This study was supported by the Heilongjiang Province application technology and development project (GA14C101-01).

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mortality[2]. With respect to iodine levels, China features unique geological conditions: 9 provinces that encompass 299 towns have drinking-water containing high levels of iodine, and goiters are prevalent in these areas[3], and there are still iodine deficient areas along the coast due to low coverage of iodized table salt. We previously conducted a cross-sectional study and demonstrated that iodine deficiency and excess coexist in China, and both conditions can cause thyroid disease or thyroid dysfunction[4]. Therefore, it is important to monitor the iodine nutrition status of the population in iodine deficient areas and excess iodine areas resulting from high iodine concentrations in drinking-water with sensitive biomarkers.

Traditionally, the urinary iodine concentration (UIC), goiter (thyroid enlargement) rate, and serum thyroid-stimulating hormone (TSH) values have been recommended measures as sensitive indicators to assess the iodine nutrition status in the population, and thyroglobulin (Tg) has been recommended as a sensitive indicator of iodine deficiency[5]. Because spot urine specimens are easy to obtain, the UIC is the most practical biochemical marker of iodine nutrition among these indicators. However, iodine is quickly metabolized in the body, and the UIC only assesses iodine intake over the past few days. In our previous study, we found that the spot urine iodine concentration was unstable over 3 consecutive days[6]. With respect to indicators of thyroid size, ultrasound is a more precise measurement of thyroid volume than palpation, but ultrasound requires specially trained operators, and the thyroid size responds slowly to changes in iodine intake. Thus, the thyroid size reflects a population's history of iodine nutrition but not its present iodine status[7]. The TSH is usually used to screen newborns, when iodine deficiency directly affects brain development, but it is seldom used to assess iodine nutrition in the entire population[8]. Moreover, Tg plays an important role in the synthesis of the thyroid hormones triiodothyronine (T3) and tetraiodothyronine (T4). Tg is a glycoprotein consisting of two 330 kD protein chains synthesized in the thyrocyte[9-10]. Tg can reportedly be stored for several weeks at room temperature in a cool and dry environment, which enables sampling in remote areas[11]. Tg can be used to measure thyroid function within several months of iodine repletion. This stability allows it to serve as a potential reliable indicator of iodine intake[5]. Previous studies have established an inverse association between the serum Tg and iodine intake in the iodine-deficient population and suggested that the serum Tg could serve as a sensitive biomarker of iodine deficiency[12-15]. Moreover, a fixed cut-off value for Tg to indicate iodine deficiency (ID) has been proposed, and this value was mainly based on data from school children obtained using dried blood spot samples[16]. In most published studies, the Tg of school children has been used as a biomarker to monitor the iodine-deficient population[17-20]. However, studies focusing on the Tg level in adults with excess iodine uptake are scarce. In the present study, the serum Tg level, thyroid enlargement and thyroid nodule as well as other possible factors influencing the serum Tg were investigated in different iodine intake areas with the aim of illuminating which factors determine the serum Tg level and confirming the hypothesis that serum Tg could be a sensitive biomarker of iodine nutrition status in adults.

SUBJECTS AND METHODS

Ethics

Research approval was obtained from the Ethics Committee of Harbin Medical University. The study was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to the survey.

Study Regions and Subjects

According to the national iodine deficiency disorders (IDD) surveillance data and water iodine surveillance data, three populations with differing iodine nutrition levels were selected in three provinces for this study. Two villages in Qingxu County and one village in the Xiaodian District of Shanxi Province were selected as areas in which residents consume water containing high levels of iodine. Five villages in Shanyin County and one village in the Xiaodian District of Shanxi Province were selected as areas where residents have sufficient iodine nutrition. Tieshangang District in Beihai City of the Guangxi Autonomous Region was selected as a coastal area with low coverage rates of iodized salt (24.29%[4]); this area is considered iodine deficient. All participants who were Han Chinese, had lived in the region for more than 10 years and were older than 18 years were eligible for recruitment. Subjects taking anti-thyroid drugs during the time of this study were excluded.