

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
ВИЩИЙ ДЕРЖАВНИЙ НАВЧАЛЬНИЙ ЗАКЛАД УКРАЇНИ
«БУКОВИНСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ»**



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Загальна редакція: професор Бойчук Т.М., професор Івашук О.І., доцент Безрук В.В.

Наукові рецензенти:

професор Братенко М.К.

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професор Юзько О.М.

д.мед.н. Годованець О.І.

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Tkachuk N.P.

**EXPRESSION OF IODINE DEFICIENCY IN PATIENTS
WITH NODULAR EUTHYROID GOITER AND POSTOPERATIVE GOITER RELAPSE**

Department of Surgery № 1

Higher State Educational Establishment of Ukraine

«Bukovinian State Medical University»

Pathological effects of iodine deficiency on thyroid are due to the fact that the deficiency of this trace element in the human body leads to a decrease in the synthesis of thyroid hormones, an increase in the level of thyroid stimulating hormone and the activation of processes that lead to excessive synthesis and release of the transformant growth factor β with subsequent uncontrolled proliferation of thyroid cells. A reliable marker for assessing the individual iodine status is the determination of serum thyroglobulin levels. Normally, thyroglobulin is not secreted in blood, and its synthesis, transport and splitting regulates thyroid-stimulating hormone. Thus, the level of thyroglobulin in the blood is the most sensitive and specific marker, which allows to detect the disruption of hormone synthesis even in the phase of compensation, that is, when the level of thyroid hormones is within the reference limits. The physiological level of thyroglobulin if the person is healthy is <10 ng / ml. However, in the presence of iodine deficiency and goiter development, its concentration is sharply increasing. For this reason, thyroglobulin is one of the markers of goiter endemic, recommended by the World Health Organization and the United Nations International Children's Emergency Fund.

The aim of the study was to determine the severity of iodine deficiency for patients with nodular and postoperative recurrent goiter.

Clinical research amounted 60 women with nodular euthyroid goiter (group I), 60 women with postoperative recurrent goiter (II group), and 30 healthy women (group III). In order to achieve homogeneity, the groups did not differ in middle age. The level of thyroglobulin in the blood was investigated by electrochemiluminescence method ECLIA (electrochemiluminescence immunoassay analysis), analyzer and test system Cobas 6000, Roche Diagnostics (Switzerland). The statistical computation of the research results was carried out using Microsoft® Office Excel spreadsheets.

By the level of thyroglobulin, the degree of deficiency is considered to be: > 40 ng / ml - severe, $20-39$ ng / ml - moderate, <20 ng / ml - mild. In the study of this indicator in the surveyed, it was found that its average content in blood serum for patients of I blood group was 57.07 ± 1.02 ng / ml; Group II before the initial operation (hemithyroidectomy or subtotal resection of the thyroid) it was 61.96 ± 0.94 ng / ml, before repeated surgery it was 41.19 ± 0.95 ng / ml, for the III group it was 14.4 ± 0.26 ng / ml; $p < 0.05$.

Thus, people of the first and second groups, were presented with a severe degree of iodine deficiency, which was even more pronounced in patients with recurrent goiter prior to the first surgery; people of the third group had a slight iodine deficiency without changes in the thyroid status and structure of the gland during ultrasound examination. It is impossible to exclude that the expressed iodine deficiency became one of the reasons for the relapse for patients of the second group. Determination of the level of thyroglobulin for patients with nodular goiter makes it possible to determine the degree of iodine deficiency in a particular patient, and to conduct adequate iodine prophylaxis in the complex of measures to prevent relapse of the disease.

Sheremet M.I.

**PROGNOSTIC MARKERS OF NODULAR ENDEMIC GOITER
WITH AUTOIMMUNE THYROIDITIS**

Department of Surgery № 1

Higher State Educational Establishment of Ukraine

«Bukovinian State Medical University»

In modern medical literature there are many publications dealing with a study of nodular endemic goiter combined with autoimmune thyroiditis (NGAIT) morphology. However, some



issues remain unresolved including that about the role of autoimmune thyroiditis (AIT) in the development of tumor processes. According to the literature, AIT leads to metaplasia processes in the thyroid epithelium, hyperplasia of lymphoid tissue, which undoubtedly can be considered as an optional precancerous condition.

The information that papillary cancer and lymphomas occur three times more frequently in patients with NEGAIT confirms this idea.

The total accuracy of clinical, instrumental and laboratory diagnostic methods for the establishment of morphological origin of nodular new growths in the TG even in the most daring conclusions does not exceed 80%. This result cannot be satisfactory either for surgeons (unjustified over diagnosis of thyroid cancer) or for endocrinologists (inadequate and ill-timed selection of patients for surgical treatment).

That is why our aim was to study the processes of proliferation and apoptosis in thyroid puncture material under NEGAIT using immunohistochemically method of investigation as well as determining the proliferative activity index.

We examined 95 women with NEGAIT. This method gives good results on the drugs that were kept after staining no more than three days. After this period, the results were unstable, which is due to the oxidization processes in some chemical compounds in the air. To start an immunohistochemically reaction we used monoclonal antibodies to the following antigens: Mouse Human Ki-67 FITC Clone MIB-1; Anti-p53 Protein Monoclonal Antibody, FITC Con-jugated, Clone DO-7; Mouse Anti-Human Apoptosis Regulator Bcl-2 (BCL2) Monoclonal, Unconjugated, Clone 124 antibody; Mouse Anti-Human CD95 Monoclonal Antibody, Unconjugated, Clone FAS18; Mouse Anti-Human CD95L Monoclonal Antibody, Unconjugated, Clone NOK-1 by Dako A/S (Denmark)

The results of immunohistochemically reaction were evaluated by means of semi quantitative analysis, proposed by A.K. Khmelnytsky, according to the intensity of color "+ -" - small "+" - poor, "++" - moderate, "+++" - pronounced. Assessment of immunoreactive cells was calculated by the formula $(Fas, FasL, Bcl-2, P53) = N1 / N2 \times 100\%$, where N1 is the number of immuno-positive cells to Fas, FasL, Bcl-2, P53 receptors, N2 - the total number of the cellular nuclei per 1 square millimeter. Assessment of the IPA was calculated by the formula $= NKi67 / N_{total} \times 100\%$ where NKi67 is the total number of nuclei immune-positive to the protein Ki67, N total is the total number of nuclei per 1 mm². Morphometric analysis was performed by means of the microscope Bresser BioScience Bino (Germany) with a digital camera Nikon DS-Fil, personal computer with installed software NIS-Elements F 3.2.

Thus, a pronounced expression of Fas and FasL on the thyroid epithelial cells, in the areas of lymphoid infiltration is indicative of the fact that in case of NEGAIT immunologically caused processes of the thyroid epithelial cells apoptosis occur. Co-expression of Fas and FasL in the areas of the lymphoid infiltration around the thyroid epithelial cells indicates that Fas and FasL are not directly involved in apoptosis of the thyroid epithelial cells, but they induce this process by producing pro-apoptotic cytokines. Increasing the number of immunoreactive cells expressing Ki67 in the area of the lymphoid infiltration and destruction of the thyroid epithelial cells is indicative of the follicular epithelium regeneration as a compensatory-adaptive response of the organ. A pronounced expression of bcl-2 in the lymphocytes prevents the cells from entering apoptosis as well as prolonging their survival time, which, undoubtedly, plays an important role in morphogenesis of the lymphoid tissue tumor dis-eases and prolonged processes of apoptosis and regeneration of the thyroid epithelium can also contribute to cancerogenesis. An increased density of p53-positive cells can be explained by mutations of p53 gene, which allows the cells to find tolerance to an apoptotic action of the immune system effectors.