# Assessment of Phospho-calcic Metabolism in Parathyroid Tumors

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*Primary hyperparathyroidism is a common hormonal disorder, third in the order of importance after diabetes and hyperthyroidism. The aim of this study is to quantify qualitatively and quantitatively the effects of parathyroid hormone hypersecretion in a group of patients diagnosed with primary hyperparathyroidism. The study, was conducted on 200 patients with hyperparathyroidism, admitted in St. Spiridon Emergency Clinical Hospital in Iasi. In the study, we noted that primary hyperparathyroidism is three times more common in women than in males, being twice as many cases in patients older than 55 years as among the youngest. The most common forms are based on genetic determinism or are associated with other endocrinopathies. The obtained results encourage us to continue the research and, at the same time, we must point out that there is a high percentage of undiagnosed people among the apparently healthy population.*

*Keywords: Primary hyperparathyroidism, hypercalcemia, parathyroid glands*

Parathyroid hormone hypersecretion characterizes abnormal activity of one or more parathyroid glands. Primary hyperparathyroidism is a common hormonal disorder, third in the order of importance after diabetes and hyperthyroidism [1,2].

In this study we analyze hyperparathyroidism in all its aspects, including general information, types of hyperparathyroidism, diagnosis procedures, and the specific treatment.

The parathyroid glands are oval in shape, and their total weight is about 30 mg in men and 35 mg in women. [3], the color varies in relation with age and blood flow. Appearance is lighter in color than the thyroid gland, varying between yellowish-reddish and reddish-brown in surgery. In women, during pregnancy, they are more voluminous and more intense colored.

Structurally, the parathyroid glands are made up of two types of cells: chief cells, which synthesize and release parathyroid hormone (PTH), and oxyphil cells which increase in number with age and have an unknown function. Parathormone controls the metabolism of calcium and phosphorus and helps in maintaining a constant relationship in blood. An adequate amount of calcium is essential for the normal functioning of the heart, the nervous system, the osteomuscular system and the kidneys [4-6].

PTH increases the body's ability to absorb calcium from food and its reabsorption to the kidneys. Calcium is deposited in bones that provide them resistance, but constant amounts of calcium are deposited and removed, depending on the body's needs. This process would not be possible without PTH intervention [7-10].

Calcium is the only mineral in the body that has a mechanism of regulation through the parathyroid glands. No other gland has this role on another mineral. When the amount of calcium rises above the normal limits, respectively, falls below the normal range, there were obeserved body disturbances and changes in the patients personality. Dysfunction of parathyroid glands is not only about osteoporosis or kidneys calculi, it is a problem related to how the patient feels mentally and that he is unable to enjoy life [11-14].

The aim of this study is to quantify qualitatively and quantitatively the effects of parathyroid hormone hypersecretion in a group of patients diagnosed with primary hyperparathyroidism.

## Experimental part

*Materials and methods*

In this study, we investigated 200 patients with hyperparathyroidism, admitted in St. Spiridon Emergency Clinical Hospital in Iasi, observing their anamnesis, symptoms, checking the investigations performed and the prescribed treatment for each patient.

The evolution of the disease has been noted by age groups, years, and genders, as well as associated comorbidities.

In the study we evaluated the diagnosis statistic of patients admitted in hospital during 01.01.2008-10.07.2018. The statistical analysis was done using Microsoft Excel.

## Results and discussions

It can be seen in the fig.1 a much higher percentage of women than men suffering from this pathology. This involves a dificult diagnosis of patients with primary hyperparathyroidism because they do not have major clinical symptoms of disease, but only increased blod levels of calcium and PTH (fig. 1).

The investigated patients with primary hyperparathyroidism had the following signs and symptoms: recurrent renal lithiasis, peptic ulcers, psychotic desorders, and less frequently encountered increased bone resorption (fig.2).

Most of the investigated patients had a single parathyroid gland affected. From the whole group 20% had two or more affected parathyroid glands (fig.3).

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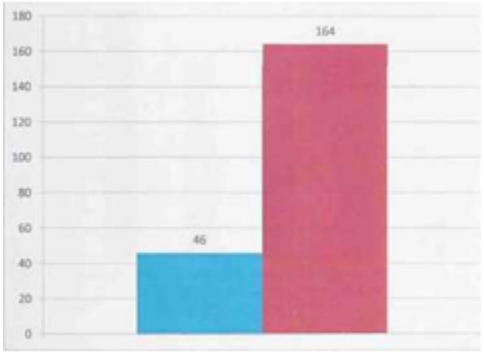


Fig.1The incidence of primary hyperparathyroidism by genders; blue is the number of men and red number of women

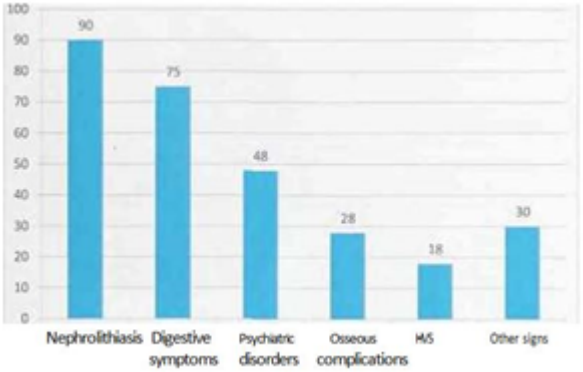


Fig.2 Symptoms associated with hyperparathyroidism

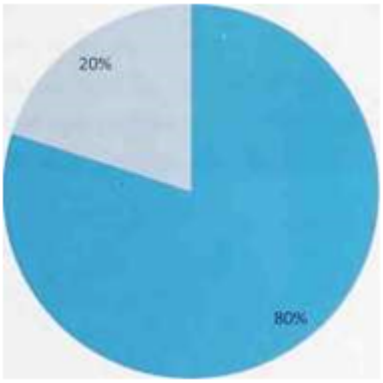


Fig.3 The incidence of hyperparathyroidism according to the number of affected glands

This gland with abnormal activity usually has a benign tumor or an adenoma. From an etiopathogenic point of view, MEN I syndrome is most commonly encountered in the causality of this pathology (fig.4).

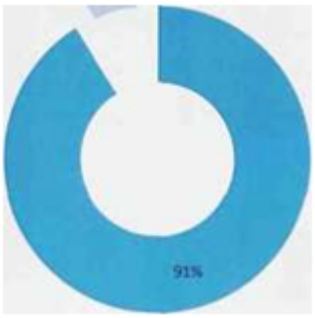


Fig.4 The incidence of MEN I versus other syndromes

Most adenomas are located in the lower parathyroid glands (fig.5).

The annual incidence of the disease is estimated at approximately 0.2% of patients over 60 years age and the prevalence is estimated to be 1% or more due to the

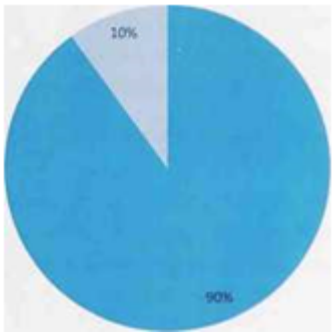


Fig.5 The incidence of adenoma localization: blue represents lower parathyroid adenomas and gray the rest

presence of a large number of asymptomatic non-diagnosed patients.

Clinical manifestations in some patients have been discrete and the disease has evolved in a benign manner for many years.

In rare cases, we noticed that the disease suddenly started or suddenly worsened, with patients experiencing severe complications. Thus, 11 cases presented severe dehydration and coma, the so-called hypercalcemiant parathyroid crisis. This disease has been more common in adults, with an apex of incidence between decades three and five, but may also appear in children or in elderly.

In approximately 20% of the patients we observed the hyperfunction of all parathyroid glands, constituting the clinical entity called parathyroid hyperplasia of the chief cells. Most of these last conditions are hereditary and are associated with other endocrine abnormalities. Some surgeons and anatomopathologists have reported that the increase in volume of several glands is common.

We have encountered hereditary hyperparathyroidism without other endocrine disorder, but more frequently it is part of a multiglandular endocrinopathy.

Patients with type I syndrome (MEN 1. Wermer syndrome) have hyperparathyroidism associated with pituitary and pancreatic tumors, frequently accompanied by peptic ulcer and gastric hypersecretion (Zollinger-Ellison syndrome).

Patients with MEN 2A syndrome have hyper-parathyroidism associated with pheochromo- cytoma and medullary thyroid carcinoma. The way of transmission of both syndromes is autosomal dominant. For patients with MEN 2A syndrome, family screening was performed to identify the first degree relatives in risk of developing the disease.

In genetic malformations in MEN 1 and MEN 2A syndromes, cytogenetic studies of tumor tissue from patients with solitary adenomas have shown that at least two molecular defects are involved in the hyperparathyroid site: increased activity of a protooncogene or growth promoting gene and loss of functionality of a growth control gene [15-17].

Adenomas are located more frequently in the lower parathyroid gland, but in 10% of patients parathyroid adenomas are located in the thymus, thyroid, pericardium or posterior wall of the esophagus. Adenomas weigh an average of 0.5-5 g, but we also encountered adenomas with the weight of 10-20 g. The adenoma is sometimes encapsulated by a crown of normal tissue.

In the case of the chief cells hyperplasia, the increase in the size of the glands can be asymmetric, so that some glands may seem normal at first view. In the presence of hyperplasia, the histological examination shows a normal appearance of the main cells and a loss of adipose tissue, even in the absence of glandular

mass growth. Therefore, the microscopic examination of biopsies from multiple glands has proven to be essential for the interpretation of preoperative findings [18-20].

In the presence of an adenoma, the other glands are usually normal, with a normal distribution of all cell types and with normal fat content.

Parathyroid carcinoma is generally less aggressive. Long-term survival without relapse is the rule if the initial intervention removes the entire gland without the capsule section [21-24]. Even in case of a relapse parathyroid carcinoma has a slow increase, with local extension to the neck. Treatment of disease recurrence remains possible. Rarely, parathyroid carcinoma is more aggressive, with distant metastases (lung, liver and bones) discovered at the initial intervention [25-28].

It is difficult to see if a primary tumor is carcinoma or not. An increasead level of mitotic images and the degree of fibrosis of the glandular stroma can mark the invasive character. Diagnosis of carcinoma is often retrospective. Hyperparathyroidism caused by a parathyroid carcinoma is not clinically different from other forms of primary hyperparathyroidism [29-32]. However, the high degree of calcium can correct the diagnosis.

## Conclusions

In the study, we noted that primary hyperparathyroidism is three times more common in women than in males, being twice as many cases in patients older than 55 years as among the youngest. The most common forms are sporadic, which are based on genetic determinism or are associated with other endocrinopathies. Our study needs to be thorough in terms of clinical follow-up and genetic testing of a larger number of subjects. The obtained results encourage us to continue the research and, at the same time, we must point out that there is a high percentage of undiagnosed people among the apparently healthy population.

## Referrences


1.GOPINATH, P., MIHAI, R. Surgery. **29**, 2011, p. 451.

2.CORDELLAT, I.M. Rheumatol Clin. **8**, 2012, p. 287.

3.JOHNSON, S.J. Journal of Clinical Pathology. **58**, no.4, 2005, p.338.

4.DE LELLIS, R.A. Tumors of the Parathyroid Gland. *Atlas of Tumor Pathology*, 3rd series, fascicle 6 Armed Forces Institute of Pathology: Washington, DC, 1993.

5.VELICESCU, C., BRANISTEANU, D., GRIGOROVICI, A., GATU, A., PREDA, C., MOGOS, V., DANILA, R. ACTA ENDOCRINOLOGICA-BUCHAREST, **11**, no.4, 2015, p.457.

6.HINGANU, M.V., SALAHORU, P., HINGANU, D. *Rev Med Chir Soc Med Nat Iasi,* **122**, no.3, 2018, p. 522.

7.SELBY, P. Clin Endocrinol (Oxf), **75**, 2011, p. 156.

8.SILVERBERG, S.J., SHANE, E., JACOBS, T.P., SIRIS, E., BILEZIKIAN, J.P. N Engl J Med. **341**, 1999, p. 1249.

9.HINGANU, M.V., HINGANU, D., COZMA, S.R., ASIMIONOAIEI-SIMIONESCU, C., SCUTARIU, I.A., IONESIE, D.S., HABA, D. Annals of Anatomy, **220**, 2018, p. 1.

10.GATU, A., VELICESCU, C., GRIGOROVICI, A., DANILA, R., MUNTEAN, V., MOGOS, S.J., MOGOS, V., VULPOI, C., PREDA, C., BRANISTEANU, D. ACTA ENDOCRINOLOGICA-BUCHAREST. **13**, no.4, 2017, p.441.

11.PALLAN, S, KHAN, A. Can Fam Physician. **57**, 2011, p.184.

12.ROTH, S.I.. Am J Pathol, **61**, 1970, p. 233.

13.SCUTARIU, M.M., HINGANU, D., MACOVEI, G., HINGANU, M.V. ROMANIAN JOURNAL OF ORAL REHABILITATION, **10**, no.4, 2018, p.186.

14.COBZEANU, B.M., IRIMICIUC, S., VAIDEANU, D., GRIGOROVICI, A., POPA, O., Mat. Plast., **54**, no.3, 2017, p.531.

15.LEMMENS, I., VAN DEVEN, W.J., KAS, K., et al. Hum Mol Genet**, 6,** 1997, p. 1177.

16.ERICKSON, L.A., JIN, L., WOLLAN, P., et al. Am J Surg Pathol, **23**, 1999, p. 288.

17.PREDA, C., VASILIU, I., BREDETEAN, O., GABRIELA, CD., UNGUREANU, MC., LEUSTEAN, EL., GRIGOROVICI, A., OPRISA, C., VULPOI, C. ENVIRONMENTAL ENGINEERING AND MANAGEMENT JOURNAL, **15**, no.4, 2016, p. 913.

18.MILAS, M., WAGNER, K., EASLEY, K.A., et al.. Surgery, **134**, 2003, p. 995.

19.ARNOLD, A., SHATTUCK, T.M., MALLYA, S.M., et al. J Bone Miner Res, **17,** 2002, p. N30–N36.

20.GRIGOROVICI, A, CHERCIU, MS, POPESCU, CM, APOSTOL, DGC, PREDA, C, CALIN, A, AELENEI, P. FARMACIA, **65**, no.1, 2017, p.29-39

21.GRIGOROVICI, A., COSTACHE, M., VELICESCU, C., SAVIN, G., CIOBANU, D., PREDA, C. CHIRURGIA, **105**, no.5, 2010, p. 669-672

22.GRIMELIUS, L., DELELLIS, R.A., BONDESON, L., et al. Parathyroid adenoma. In: DeLellis RA, Lloyd RV, Heitz PU, Eng C (eds). Pathology and Genetics of Tumours of Endocrine Organs. World Health Organization Classification of Tumours, IARC Press: Lyon, France, 2004, pp 128–132.

23.SCHNEIDER, D.F., MAZEH, H., CHEN, H., SIPPEL, R.S. Ann Surg., **259**, 2014, p. 563.

24.O'CONNELL, R.L., AFORS, K., THOMAS, M.H. WJOES, **3**, 2011, p.107.

25.SNOVER D, FOUCAR K. Am J Clin Pathol, **75**, 1981, p. 345.

26.VARGAS, M.P., VARGAS, H.I., KEINER, DE,., et al. Mod Pathol, 10, 1997, p.12.

27.ALBRIGHT, F., BLOOMBERG, E., CASTLEMAN, B., et al.. Arch Int Med , 54, 1934, p.35–329.

28.CARNEIRO, D.M.,SOLORZANO, C.C., IRVIN, III G, L., J Am Coll Surg, **199**, 2004, p. 849.

29.HINGANU, D., HINGANU, M.V., MIHALCEANU, E., CALIN, A.M., PANGAL, A., COSTACHESCU, G., ROMILA, A., Rev. Chim. (Bucharest), **69**, no.3, 2018, p. 714

30.BISKOBING, D.M. Endocrine Pract, **16**, 2009, p.112.

31.DE LELLIS, R.A. Adv Anat Pathol, **12**, 2004, p. 53.

32.SANDELIN, K., TULLGEN, D., FARNEBO, O. World J Surg, **18**, 1994, p. 594.



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