Correlation of hyperinsulinemia with diseases of the gastrointestinal tract and the level of electrolytes in blood serum

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Abstract

The aim of our research is to determine the correlation of insulin resistance with diseases of the gastrointestinal tract and the level of trace elements in blood serum.

Metods: The study cohort included a total of 413 patients aged 20–75 years (mean age 37.3 ± 11.4 years) referred to the National Institute of Endocrinology from 2017 to 2019The cohort included 120 men and 293 women . A retrospective selection of the study population was made based on patient history, where hyperinsulinemia was diagnosed.

We considered fasting hyperinsulinemia in blood serum as compensatory hyperinsulinemia during insulin resistance. On the basis of which, we included individuals with hyperinsulinemia in the study group of insulin resistance, while the control group consisted of 161 subjects with normoinsulinemia.

Results: In the study group, compared to the control group, there was a significant decrease in the level of zinc (74.50±14.43 vs 88.52±14.63; p<0.0001) and also an increase in the level of transaminases – ALT(37.51±29.96 vs 28.49±25.89; p=0.0019) and AST(27.23±17.94 vs 21.28±8.80; p=0.0001).

- The incidence of gastrointestinal tract diseases did not show a positive correlation with the level of insulin in blood serum
- Hyperinsulinemia shows a reliable positive correlation with decreased zinc levels in the blood serum.

Keywords: insulin, hyperinsulinemia, gastrointestinal tract, Zn

ჰიპერინსულინემიის კორელაცია კუჭ-ნაწლავის ტრაქტის დაავადებებთან და სისხლის შრატში ელექტროლიტების დონესთან

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აბსტრაქტი

ჩვენი კვლევის მიზანია დადგინდეს ინსულინის რეზისტენტობის კორელაცია კუჭ-ნაწლავის ტრაქტის დაავადებებთან და სისხლის შრატში მიკროელემენტების დონესთან.

მეთოდები: კვლევის კოჰორტა მოიცავდა სულ 20-75 წლის 413 პაციენტს (საშუალო ასაკი 37.3 ± 11.4 წელი), რომლებიც მიმართეს ენდოკრინოლოგიის ეროვნულ ინსტიტუტს 2017 წლიდან 2019 წლამდე. კოჰორტა მოიცავდა 120 მამაკაცს და 293 ქალს. საკვლევი

პოპულაციის რეტროსპექტული შერჩევა განხორციელდა პაციენტის ისტორიის საფუძველზე, სადაც დადგინდა ჰიპერინსულინემია.

ჩვენ განვიხილეთ უზმოზე ჰიპერინსულინემია სისხლის შრატში, როგორც კომპენსატორული ჰიპერინსულინემია ინსულინრეზისტენტობის დროს. რის საფუძველზეც ჩვენ ჩავრთეთ ჰიპერინსულინემიის მქონე პირები ინსულინრეზისტენტობის საკვლევ ჯგუფში, ხოლო საკონტროლო ჯგუფი შედგებოდა ნორმოინსულინემიის მქონე 161 სუბიექტისგან.

შედეგები: საკვლევ ჯგუფში, საკონტროლო ჯგუფთან შედარებით, დაფიქსირდა თუთიის დონის მნიშვნელოვანი შემცირება (74,50+14,43 vs 88,52+14,63; p<0,0001) და ასევე გაიზარდა ტრანსამინაზების დონე – ALT(37,51+). 29.96 vs 28.49+25.89; p=0.0019) და AST(27.23+17.94 vs 21.28+8.80; p=0.0001).

• კუჭ-ნაწლავის ტრაქტის დაავადებების სიხშირე არ აჩვენებდა დადებით კორელაციას სისხლის შრატში ინსულინის დონესთან

• ჰიპერინსულინემია აჩვენებს საიმედო დადებით კორელაციას სისხლის შრატში თუთიის დონის დაქვეითებასთან.

საკვანძო სიტყვები: ინსულინი, ჰიპერინსულინემია, ტრანნსამინაზები,Zn.

Introduction

Epidemiological assessment of insulin resistance is usually measured by the prevalence of metabolic syndrome [1]. Metabolic syndrome includes risk factors for type 2 diabetes cardiovascular disease [2] and Hyperinsulinemia is the most common cause of diffuse goiter and the heterogeneous structure of the thyroid [3]. Metabolic syndrome is a combination of metabolic disorders, which includes arterial hypertension, central obesity, insulin resistance and atherogenic dyslipidemia. Metabolic syndrome, also called "insulin resistance syndrome," "Syndrome X," and "the deadly quartet," is increasingly recognized as an important cardiovascular risk factor, even without type 2 diabetes [4, 5, 6]. Excessive accumulation of adipose tissue in the human body leads to insulin resistance, which plays a crucial role in the development of metabolic syndrome [7]. Insulin resistance leads to hyperinsulinemia, which is accompanied by an increase in the level of glucose in the blood serum, because the increased demand for insulin due to insulin resistance exceeds the ability of the beta cells of the pancreas to release adequate amounts of insulin, which

ultimately contributes to the development of type 2 diabetes mellitus [8]. Insulin resistance is associated with excessive accumulation of adipose tissue in the human body [9,10].

In developed countries, the prevalence of metabolic syndrome in the adult population has increased to 20-25%, and its frequency is increasing over time in all age groups [11,12].

As the incidence of insulin resistance is increasing, we were interested in studying the correlation of insulin resistance with diseases of the gastrointestinal tract and the level of trace elements in blood serum.

Methods and Material

The study cohort included a total of 413 patients aged 20–75 years (mean age 37.3 ± 11.4 years) referred to the National Institute of Endocrinology from 2017 to 2019The cohort included 120 men and 293 women . A retrospective selection of the study population was made based on patient history, where hyperinsulinemia was diagnosed.

We considered fasting hyperinsulinemia in blood serum as compensatory hyperinsulinemia during insulin resistance. On the basis of which, we included individuals with hyperinsulinemia in the study group of insulin resistance, while the control group consisted of 161 subjects with normoinsulinemia.

Inclusion Criteria: Hyperinsulinemia

Exclusion Criteria: pregnancy, hyperthyroidism, hypothyroidism, diabetes type 2; Type 1 diabetes mellitus, estrogen or metformin treatment, gastric bypass, treatment, patients with bariatric intervention, surgical patients, chronic liver and kidney failure, oncological diseases, neurological diseases, hidden social life conditions.

Study variables included: age, sex, social status, body mass index (BMIcm/m2), clinical signs observed included: Flatulence, abdominal pain, gastritis, gastric and duodenal ulcer disease, gastrointestinal oncological disease, ionized calcium, zinc, chlorine, phosphorus, alanine aminotransferase, aspartamino transferase.

sweating, dry skin, hair loss, brittle nails, headache, dizziness, fatigue, mood and appetite. Laboratory tests included: vitamin D, TSH, anti-TPO and thyroid ultrasonography

Statistical Analysis:

Biochemical analyzes were performed -Tosoh AIA-900(Fluorescence enzyme immunoassay). Quantitative values are presented as the mean ± SD and qualitative values as absolute values and percentages. For qualitative variables the difference between groups was analyzed by Fishers' exact test,while for quantitative variables it was analyzed by the _Student's t-test. Correlations between quantitative factors determined by the Pearson correlation coefficient, and between qualitative factors using – Spearmans' correlation analysis. Sensitivity and specificity was calculated by ROC analysis. Linear regression analysis and other statistical tests were performed using SPSS23 software.

Among the patients studied by us, insulin resistance was detected in 252 persons, the rate of insulin resistance is significantly higher in women than in men - respectively 79.5% and 65.49% (p=0.0021).

Results

The distribution of patients by age is shown in Figure 1

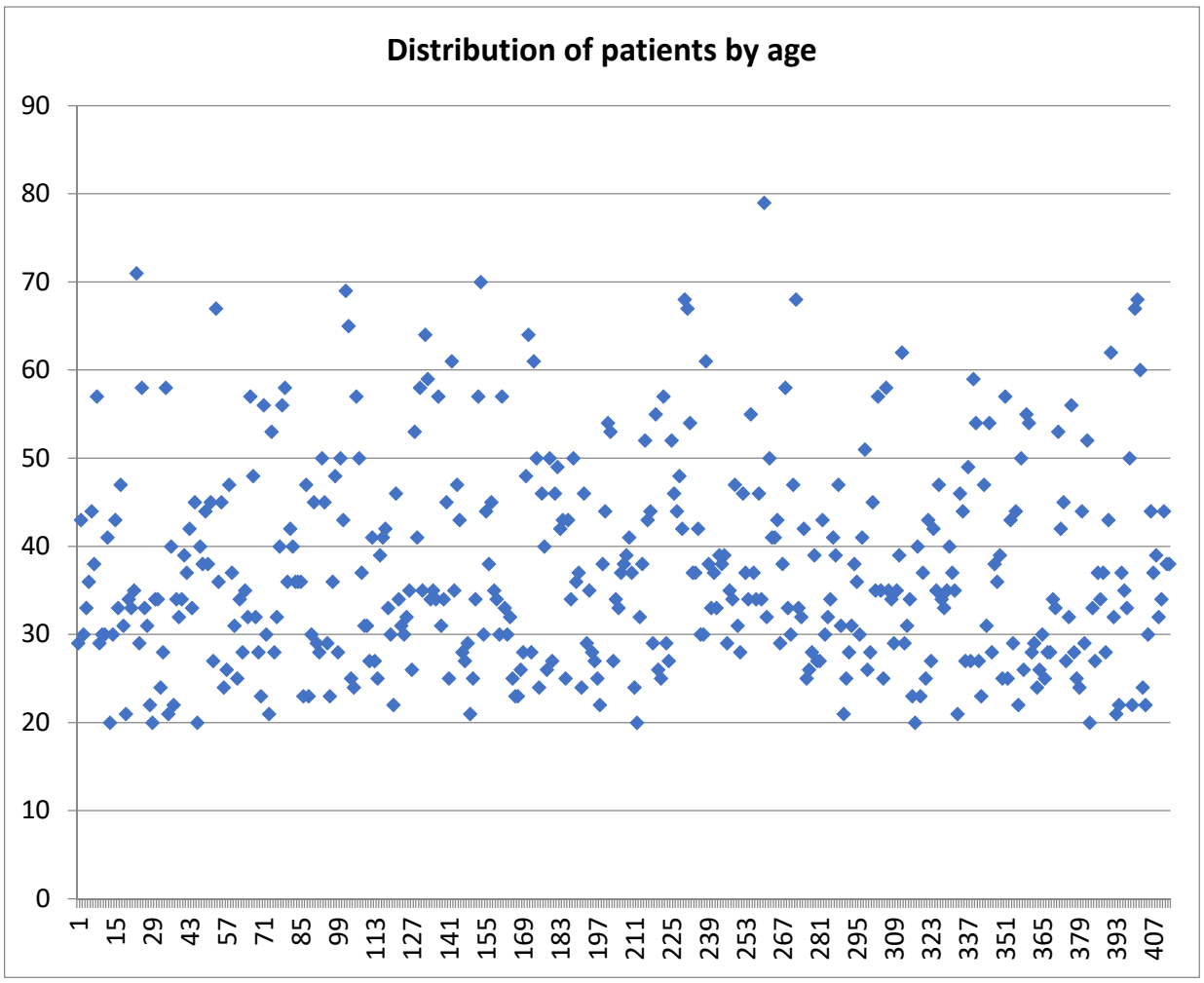

Figure 1

The average age of the patients was 37.3±11.4 years, the range was 20-75 years.

There were 120 men and 293 women among the examined persons.

In the study group, compared to the control group, the incidence of gastrointestinal diseases did not change (Figure 2).

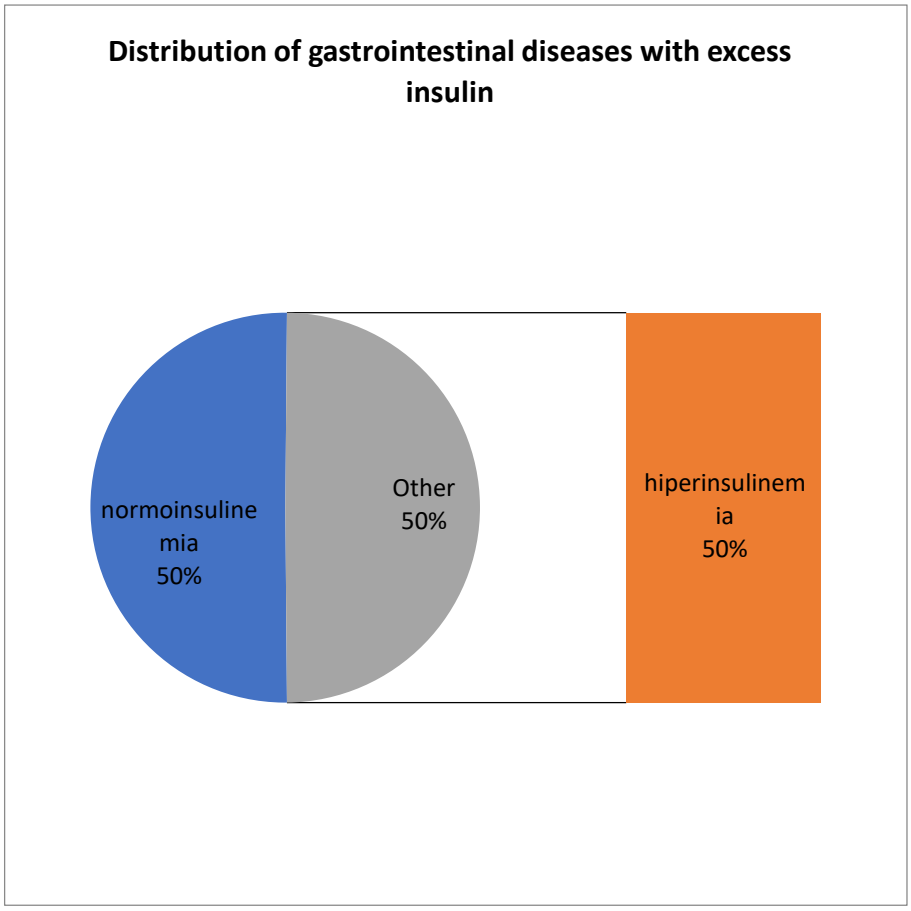

Figure 2

Table 1 shows the biochemical characteristics of insulin resistance

Table 1. Evaluation of biochemical characteristics during insulin resistance

	Control group			Study group			t	p
	N	Mean	SD	N	Mean	SD		
Fasting glucose (80-110 mg/dl)	161	99.36	15.68	253	101.54	19.82	-1.24	0.2147
Zn (80-120)mg/dl	159	88.52	14.63	250	74.50	14.43	9.50	<0.0001
Ca(1.15-1.3)	159	1.20	0.07	251	1.23	0.32	-1.47	0.1421
Mg(1.7-2.5)	156	1.97	0.24	237	2.86	13.91	-0.98	0.3285
K(80-120)	157	4.15	0.36	240	4.13	0.40	0.69	0.4904
P(2.5-5)	150	3.68	0.68	233	3.58	0.81	1.34	0.1817

Cl(98-110)	151	103.74	3.54	233	103.39	8.71	0.54	0.5881
ALT	159	28.49	25.89	252	37.51	29.96	-3.13	0.0019
AST	159	21.28	8.80	252	27.23	17.94	-3.90	0.0001

In the study group, compared to the control group, there was a significant decrease in the level of zinc and also an increase in the level of transaminases.

Discussion:

According to some studies, obesity is associated with insulin resistance and is a known risk factor for esophageal, gastric cardia, and colorectal carcinoma [13,14]. According to some authors, on the other hand, disruption of the microbiota flora in the gastrointestinal tract may contribute to the development of metabolic syndrome risk factors [15, 16]. According to our research, no oncological disease of the gastrointestinal tract was detected in the study group. Also, there was no significant difference between the study and control groups in terms of the incidence of gastrointestinal diseases. Some authors suggest that insulin resistance can cause liver dysfunction [17]. According to our study, a significant increase in the level of transaminases was noted in the study group compared to the control group.

Zinc (Zn) is an important mineral in the human body [18]. Zn plays a crucial role in the storage of insulin in the granules inside the beta cells of the pancreas[19]. According to some studies, zinc deficiency may cause various metabolic disorders [20]. According to some studies, magnesium deficiency is more common in people with obesity, type 2 diabetes, and metabolic syndrome, both in adults and in children [21, 22, 23]. Some authors believe that consuming foods high in calcium may reduce the risks of metabolic syndrome[24]. According to some authors, low serum potassium levels in perimenopausal women are associated with an increased risk of metabolic syndrome [25]. According to our study, there was no significant difference between the blood serum levels of potassium, calcium, phosphorus and chlorine in the study group compared to the control group. According to our study, there was a significant decrease in zinc levels in the control group compared to the study group.

Conclusions:

- The incidence of gastrointestinal tract diseases did not show a positive correlation with the level of insulin in blood serum
- Hyperinsulinemia shows a reliable positive correlation with decreased zinc levels in the blood serum.

References

1. Freeman AM, Pennings N. Insulin Resistance. 2021 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 29939616.
2. Sperling LS, Mechanick JI, Neeland IJ, Herrick CJ, Despres JP, Ndumele CE, Vijayaraghavan K, Handelsman Y, Puckrein GA, Araneta MR, et al. (2015). The CardioMetabolic Health Alliance: Working Toward a New Care Model for the Metabolic Syndrome. *J Am Coll Cardiol* 66, 1050–1067.
3. Lomtadze N, Giorgadze E, Janjgava S, Kacharava T, Taboridze I. "The relationship between Insulin Resistance and Thyroid Volume in Georgia". Endocr Metab Immune Disord Drug Targets. 2023 Feb 20.
4. Grundy SM, Hansen B, Smith SC, Jr, et al. American Heart Association, National Heart, Lung, and Blood Institute, American Diabetes Association. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. *Arterioscler Thromb Vasc Biol* 2004; 24(2): e19–e24
5. Heng T.O. Cardiac syndrome X versus metabolic syndrome X. *Int. J. Cardiol.* 2006;119:137–138.
6. Sarafidis PA, Nilsson PM. The metabolic syndrome: a glance at its history. *J Hypertens.* 2006;**24**(4):621–626.
7. Swarup S., Zeltser R. *Metabolic Syndrome.* StatPearls Publishing; Treasure Island, FL, USA: 2020
8. Defronzo R.A. Banting Lecture. From the triumvirate to the ominous octet: A new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes.* 2009;58:773–795.

9. Freeman AM, Pennings N. Insulin Resistance. 2021 Nov 15. In: StatPearls [Internet].
10. Czech MP. Insulin action and resistance in obesity and type 2 diabetes. Nat Med. 2017 Jul 11;23(7):804-814.
11. Cano-Ibáñez N., Gea A., Martínez-González M.A., Salas-Salvadó J., Corella D., Zomeño M.D., Romaguera D., Vioque J., Aros F., Wärnberg J., et al. Dietary diversity and nutritional adequacy among an older Spanish population with metabolic syndrome in the PREDIMED-plus study: A cross-sectional analysis. *Nutrients.* 2019;11:958.
12. Fahed G, Aoun L, Bou Zerdan M, Allam S, Bou Zerdan M, Bouferraa Y, Assi HI. Metabolic Syndrome: Updates on Pathophysiology and Management in 2021. Int J Mol Sci. 2022 Jan 12;23(2):786.
13. Aaronson S. Growth factors and cancer. *Science (Washington, DC)* 1991; 1146– 53.
14. Martinez J, Sanchez-Paya J, Palazon JM, Suazo-Barbona J, Robles-Diaz G, Perez-Mateo M. Is obesity a risk factor in acute pancreatitis? A meta-analysis. *Pancreatology* 2004; 4: 42– 8
15. Cani PD, et al. Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes.* 2007;**56**(7):1761–1772. doi: 10.2337/db06-1491.
16. Dabke K, Hendrick G, Devkota S. The gut microbiome and metabolic syndrome. J Clin Invest. 2019 Oct 1;129(10):4050-4057
17. Utzschneider KM, Kahn SE. Review: the role of insulin resistance in nonalcoholic fatty liver disease. *J Clin Endocrinol Metab* 2006;91:4753–4761
18. Xia S., Zhang X., Zheng S., Khanabdali R., Kalionis B., Wu J., Wan W., Tai X. An Update on Inflamm-Aging: Mechanisms, Prevention, and Treatment. *J. Immunol. Res.* 2016;2016:8426874.
19. Chimienti F., Favier A., Seve M. ZnT-8, a pancreatic beta-cell-specific zinc transporter. *Biometals.* 2005;18:313–317. doi: 10.1007/s10534-005-3687-9.
20. Grüngreiff K., Franke D., Lössner B., Abicht K., Kleine F.D. Zinc deficiency-A factor in the pathogenesis of hepatic encephalopathy. *Z. Gastroenterol.* 1991;29:101–106.
21. Jiang S., Ma X., Li M., Yan S., Zhao H., Pan Y., Wang C., Yao Y., Jin L., Li B. Association between dietary mineral nutrient intake, body mass index, and waist circumference in U.S. Adults using quantile regression analysis NHANES 2007–2014. *PeerJ.* 2020;8:e9127. doi: 10.7717/peerj.9127.

22. Kelly O.J., Gilman J.C., Kim Y., Ilich J.Z. Macronutrient Intake and Distribution in the Etiology, Prevention and Treatment of Osteosarcopenic Obesity. *Curr. Aging Sci.* 2016;10:83–105.
23. Piuri G, Zocchi M, Della Porta M, Ficara V, Manoni M, Zuccotti GV, Pinotti L, Maier JA, Cazzola R. Magnesium in Obesity, Metabolic Syndrome, and Type 2 Diabetes. Nutrients. 2021 Jan 22;13(2):320.
24. Moore-Schiltz L., Albert J.M., Singer M.E., Swain J., Nock N.L. Dietary intake of calcium and magnesium and the metabolic syndrome in the National Health and Nutrition Examination (NHANES) 2001–2010 data. *Br. J. Nutr.* 2015;114:924–935.
25. Cybulska AM, Schneider-Matyka D, Bosiacki M, Chlubek D, Panczyk M, Grochans E. The Levels of Bioelements in Postmenopausal Women with Metabolic Syndrome. Nutrients. 2022 Oct 2;14(19):4102.