American Journal of Interdisciplinary Research and Development
ISSN Online: 2771-8948
Website: www.ajird.journalspark.org
Volume 33, October - 2024

# METABOLIC COMPLICATIONS OF GROWTH HORMONE DEFICIENCY IN PATIENTS WITH ISCHEMIC HEART DISEASE

Urmanova Yulduz Makhkamovna
Doctor of Medical Sciences, Professor of the Department of Clinical Disciplines, Alfraganus University
Office address: Tashkent, 100190, Yukori Karakamysh street 2 A
Tel mob +99890-9040165, email yulduz.urmanova@mail.ru

**Abstract**
In this article, the authors discussed the results of investigation of 21 adults with ischemic heart disease (IHD) and metabolic syndrome with growth hormone deficiency syndrome in adults (GHD). The investigation of hormonal status disorders found of the level of STH and IGF-1 in blood plasma. It was established that frequency of GHD in patients with IHD of both groups was 15 cases from 21 patients (71.4%). Besides that, 8 patients from 15 (53.3%) with GHD have low levels of GF-1 too. The levels of STH was in range from 0.15 ng/ml to 0.53 ng/ml in 13 (86.6%) patients from 15, which noted the high frequency of low levels of STH in both groups. And the levels of IGF-1 - in range rom 58 ng/ml to 120 ng/ml in 10 (50%) from 20 patients.

**Keywords**: Adult growth hormone deficiency (AGHD), coronary heart disease (CHD), metabolic syndrome (MS)

## Introduction

One of the first authors to publish for the first timeMore than 25 years ago, research onadult growth hormone deficiency (The first person to study the DHRV problem was Professor A.B. Grossman with his work on the effect of radiation therapy on pituitary tumors, and he noted that the only early-onset endocrinopathy was a deficiency of growth hormone: “I did not attach much importance to this because “it had no clinical significance, since the patients were adults” [7]. At present, the problem of DHRV is the subject of many studies by Russian and foreign authors. Thus, the role of growth hormone deficiency in the development of coronary heart disease in patients with type 2 diabetes mellitus (DM) was shown in the work of V.N. Shchukina, 2006 [3], which showed that the nature of the course of coronary heart disease and its progression in patients with type 2 DM are associated with insufficient secretion of growth hormone. She notes that GHRD plays a leading role in the development of dyslipoproteinemia, which underlies atherosclerosis, and the development and progression of “late” micro- and macrovascular complications of diabetes, decreased physical performance and changes in intracardiac hemodynamics.

In patients with adult growth hormone deficiency syndrome (AGHD)There are several metabolic abnormalities and it has been found that there is increased cardiovascular morbidity and mortality in patients with GHD with hypopituitarism [1-3] may be related to missing metabolic effects of GH. Johannsson and Bengtsson [8,9] indicated that the adult phenotype of DHRV shares features with metabolic syndrome (MS), such as abdominal obesity, dyslipidemia, and insulin resistance, which are a group of risk factors for cardiovascular disease (CVD) and type 2 diabetes.

Accordingly, in patients withIn overweight or obese individuals, metabolic disorders typical of MS could be associated with DHRV, but could also exist independently of DHRV. In such a situation, cause and effect can overlap; on the one hand, obesity and metabolic disorders can be consequences of DHRV, while on the other, obesity itself can cause endocrine disorders.[5-7].This aspect was taken into account in the biochemical diagnosis of GHD, and the growth hormone (GH) response in stimulation tests was standardized depending on the degree of existing obesity.[10-13].However, obesity itself can disrupt not only GH secretion, but also the clinical manifestations of GH syndrome, as well as the effects of GH therapy.

All this indicates the relevance of the chosen topic and served as the reason for conducting this study.

**The aim of the study is** to study the metabolic outcomes of GHD in patients with coronary heart disease (CHD).

## Material and Methods of Research

We examined 21 adult patients with coronary heart disease and metabolic syndrome (MS). Of these, 13 were men (61.9%) and 8 were women (38%). The average age was 58.0 years for men and 58.2 years for women. The duration of the disease ranged from 2 months to 25 years. The control group consisted of 20 healthy individuals of both sexes of the corresponding average age.

The research methods included: 1) general clinical (examination of endocrine, neurological and ophthalmological status, anthropometry - height, weight, WC, HC, BMI, assessment of DGRV according to the standard international questionnaire), 2) instrumental (fundus, visual acuity, ECG, echo-ECG, hM-ECG, ultrasound of internal organs, etc.), 3) hormonal blood tests (STH, IGF-1, LH, FSH, PRL, TSH, ACTH, prolactin, testosterone, estradiol, progesterone, cortisol, T3, T4), 4) general clinical and biochemical blood tests (total protein, fibrinogen, PTI, ALT, AST, total zolesterol, LDL, VLDL, HDL, triglycerides, calcium, coagulogram, glucose. blood, glycated hemoglobin, total bilirubin, direct bilirubin, urea and creatinine, ASLO, CRP, glucose tolerance test, etc.) and urine.

Lipid metabolism study: total cholesterol and TG were determined using tests from the company "Randox» on the autoanalyzer «Centrifichem-600», HDL-C — on the autoanalyzer «Technicon AAP» (USA) after precipitation from plasma LDL and VLDL with phosphotungstic acid. The level of LDL-C and VLDL-C was calculated according to the formulas of W. Friedwald.

All patient data were entered into the computer database we created, "Volumetric formations of the hypothalamic-pituitary system with growth hormone deficiency," for further statistical processing (Intellectual Property Agency of the Republic of Uzbekistan, Certificate of Registration BGU 00263 dated 25.03. 2011 Tashkent, Shakirova M.Yu., Urmanova Yu.M.)

The obtained data were processed using the computer programs Microsoft Excel and STATISTICA_6. Differences between groups were considered statistically significant at P□ 0.05.

The reliability of differences in the level between groups was assessed by the value of the confidence interval and the Student's criterion (p). Differences were considered statistically significant at $p < 0.05$.

**Research results and their discussion.**

Table 1 shows the distribution of patients by gender and age.

**Table 3. Distribution of patients by gender and age (according to WHO)**

| Age, years | Number of men (%) | Number of women (%) |
|---|---|---|
| 16 – 29 | - | - |
| 30-44 | - | 1 (12.5%) |
| 45-59 | 9 (69.2%) | 4 (50%) |
| 60-74 | 4(30.7%) | 3 (38%) |
| 75 and Art. | - | - |
| Total: 21 | 13 (61.9%) | 8 (38%) |

Table 1 shows that most often the patients were aged 45 to 59 years - 13 patients (61.9%), that is, still of working age.

Next, we studied the clinical and anamnestic characteristics of the patients.

**Table 2. Distribution of patients into groups**

| Patient groups | Number of men (% ) | Number of women (%) |
|---|---|---|
| 1. IHD. Angina pectoris FCII | 2 (15.4%) | 2 (25%) |
| 2. IHD. Angina pectoris FC III | 11 (84.6%) | 6 (75%) |
| **Total:** | **13** | **8** |

Table 2 shows the distribution of patients into groups depending on the severity of the underlying disease. Patients were divided into 2 main groups: Group 1 – patients with coronary artery disease. Angina pectoris. FCII – 4 patients (19.0%), group 2 -patients with ischemic heart disease. Angina pectoris. FCIII – 17 (81.0%).

The study of the anamnesis showed that in 10 (47.6%) cases of our patients postinfarction cardiosclerosis was established, in 2 (9.5%) cases coronary artery stenting was performed,

in 1 (4.7%) aortocoronary bypass grafting. Table 3 provides characteristics of concomitant diseases and complications of patients.

**Table 3. Characteristics of concomitant diseases and complications of the underlying disease in patients by groups**

| Associated diseases and complications | 1 group (%) | 2 group (%) |
|---|---|---|
| 1. Obesity 1-2 tbsp. | 4 (100%) | 16 (94.2%) |
| 2. Hypertension. 2-3 st. | 3 (75%) | 15 (88.2%) |
| 3. Diabetes mellitus type 2. | 2 (50%) | 5 (29.4%) |
| 4. Osteochondrosis of the spine | 1 (25%) | 6 (35.2%) |
| 5. Chronic cholecystitis | 1 (25%) | 1 (5.9%) |
| 6. Chronic pyelonephritis | | 4 (23.5%) |
| 7. Spontaneous hypothyroidism | 1 (25%) | 1 (5.9%) |
| 8. Hypochromic anemia 2nd degree. | - | 1 (5.9%) |
| 9. Chronic gastritis | 1 (25%) | 1 (5.9%) |
| 10. Peptic ulcer of the 12th p.c. | - | 1 (5.9%) |
| 11. CHF 1-2 st. | 3 (75%) | 15(88.2%) |
| 12. Discirculatory encephalopathy 1-2 st. | 2 (50%) | 14 (82.3%) |
| 13. Diabetic encephalopathy 1-2 st. | - | 3 (17.6%) |
| 14. Consequence of ischemic stroke | - | 1 (5.9%) |
| 15. Diabetic polyneuropathy | 1 (25%) | 1 (5.9%) |
| 16. Left ventricular (LV) aneurysm | - | 1 (5.9%) |
| 17. Thrombus in the LV cavity | - | 1 (5.9%) |
| 18. Chronic renal failure 2 | - | 1 (5.9%) |
| 19. Ventricular extrasystole | 2 (50%) | - |
| 20. Transient ischemic attacks | - | 1 (5.9%) |

As can be seen from Table 3, among the metabolic disorders in the examined patients there were such as obesity of 1-2 degrees - in 20 patients out of the total number of patients (95.2%), diabetes mellitus type 2 - in 7 (33.3%), etc. Among the complications of the underlying disease, the following dominated: chronic heart failure (CHF) 1-2 st - in 18 patients out of 21 (85.7%), as well as discirculatory encephalopathy - in 16 (76.2%). Among the concomitant diseases, the most common were hypertension - in 18 (85.7%), widespread osteochondrosis of the spine - in 7 (33.3%).

The study of the objective status of patients showed the following changes in anthropometric indicators, which are shown in Table 4.

American Journal of Interdisciplinary Research and Development
ISSN Online: 2771-8948
Website: www.ajird.journalspark.org
Volume 33, October - 2024

**Table 4. Average values of anthropometric indicators of patients.**

| No. | Indicators | Norm (WHO) | Men | | Women | |
|---|---|---|---|---|---|---|
| | | | 1 gr | 2 gr | 1 gr | 2 gr |
| 1 | Height standing, cm | M up to 174.7<br>W up to 162.2 | 175.2 ± 9.5 | 170.2±8.3 | 155.5 ± 3.7 | 156.2±3.5 |
| 2 | Weight, kg | M not <60<br>F not < 55 | 86.5 ± 3.6 | 97.9 ± 4.1 | 82.5 ± 2.5 | 79.16 ± 6.3 |
| 3 | Waist size (cm) | M to 94<br>F up to 80 | 104.5 ± 8.7 | 112.63 ± 8.5 | 99.2 ± 3.3 | 110.83 ±9.1 |
| 4 | Hip volume (cm) | M to 94<br>F up to 90 | 103.5 ± 8.4 | 111.81±9.1 | 112.5 ± 8.9 | 118.16 ±8.5 |
| 5 | OT/OB | M = 1<br>W up to 0.8 | 1.00 ± 0.02 | 1.00 ± 0.02 | 0.85 ± 0.04 | 0.93 ± 0.05 |
| 6 | BMI, kg/m2 | 18.5- 24.9 | 28.2 ± 3.6 | 33.87 ± 4.4 | 34.4 ± 2.5 | 32.57 ± 2.7 |

*Data for height and weight are taken from I.I. Dedov “Somatotropic insufficiency”, Moscow, 1998, 302 p.

According to the analysis of average values of anthropometric parameters, men of group 1 had pre-obesity - BMI within 28.2 kg/m2, women of group 1 had grade 1 obesity - BMI = 34.4, and both men and women had grade 1 obesity (respectively, BMI 33.87/32.57 kg/m2), which increases the risk of concomitant diseases. It should be noted that WC in both men and women of both groups was significantly increased ($P < 0.05$) and was highest in patients of both sexes of group 2. All this indicates an increased risk of developing metabolic complications in both groups of patients.

Next, we studied the neuroendocrine symptoms of patients. In order to identify AGHD, we used the Quality of Life for Adult Growth Hormone Deficiency (QoL AGHD) questionnaire (18). These data are presented in Table 5.

**Table 5.** Results of the survey of patients using the questionnaire for the development of gastrointestinal tract disease in adults

| No. | Number of respondents in the group | Control | Average score | Reliability of differences, p |
|---|---|---|---|---|
| 1 | 1 group (n = 4) | 7.3± 0.4 | 9.75± 0.4 | P > 0.5 |
| 2 | 2 group (n=17) | | 17.3± 0.3 | P < 0.05 |

Using the questionnairefor the identification of AGHD (QoL AGHD) revealed during the preliminary survey a reliable decrease in scores in 15 (71.4%) patients, that is, in the overwhelming majority of patients.

American Journal of Interdisciplinary Research and Development
ISSN Online: 2771-8948
Website: www.ajird.journalspark.org
Volume 33, October - 2024

As can be seen from Table 5, the study of quality of life using the GHRD questionnaire revealed its impairment in both groups of patients, which indicates an increased likelihood of growth hormone deficiency in both groups of patients.

The study of hormonal status revealed significant disturbances in the concentration of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) in blood plasma, presented in Table 6.

**Table 6. Average GR values**and IGF-1 in patient groups

| No. | Hormones | Control | Group I n=4 | R | II group n=17 | R |
|---|---|---|---|---|---|---|
| 1 | GRng/ml | 3.5 ± 0.3 | 1,1± 0.2 | < 0.05 | 0.2± 0.01 | < 0.05 |
| 2 | IGF-1,ng/ml | 485 ± 9.8 | 156.3± 3.3 | > 0.5 | 129.7± 7.5 | < 0.05 |

P – reliability of differences compared to the norm

It was found that the frequency of GHD in the examined patients with coronary heart disease of both groups was 15 cases out of 21 (71.4%). At the same time, 8 (53.3%) patients with laboratory-established GHD showed a reliable decrease in the concentration of IGF-1 in the blood plasma. It should be emphasized that GH levels fluctuated within the range from 0.15ng/mlup to 0.53ng/mlin 13 (86.6%) of 15 patients overall, indicating a predominance of low basal GH concentrations. And IGF-1 levels were within 58ng/mlup to 120ng/ml in 10 (50%) of 20 patients.

Thus, reliable differences in the average concentration and GH compared to the norm were found in both groups, especially in the 2nd. At the same time, a reliable decrease in the average values of IGF-1 in blood plasma was found only in the 2nd group of patients. As is known, the content of IGF-1, namely a decrease in its level from normal values, is a marker of GHD in adults. Therefore, GHD in adults was most reliably observed in patients of the 2nd group.

Next, we analyzed the correlation between the GHD and the GHD questionnaire data in order to study the effectiveness of its use. These data are presented in Table 7.

**Table 7. Correlation between GH deficiency, IGF-1 and questionnaire data.**

| Hormones | Control | Group I n=4 | R | II group n=17 | R |
|---|---|---|---|---|---|
| GRng/ml | 3.5 ± 0.3 | 1,1± 0.2 | < 0.05 | 0.2± 0.01 | < 0.05 |
| IGF-1,ng/ml | 485 ± 9.8 | 156.3± 3.3 | > 0.5 | 129.7±7.5 | < 0.05 |
| Questionnaire data | 7.3± 0.4 | 9.75± 0.4 | > 0.5 | 17.3±0.3 | < 0.05 |
| Number of cases with significant correlation between GH deficiency, IGF-1 and questionnaire | - | 1 | < 0.05 | 7 | < 0.05 |

P – reliability of differences compared to the norm

The analysis of the obtained results showed that a reliable correlation between significantly reduced levels of GH, IGF-1 in blood plasma and a low score on the GHD in adults questionnaire was found in 8 patients of both groups, which is 38.0% of the total number of patients, including 1 (25%) patient from Group 1 and 7 (41.2%) patients from Group 2. It should be noted that out of 15 patients with laboratory-confirmed GHD in adults, this correlation was found in 53.3%. Thus, the effectiveness of the questionnaire in identifying GHD in adults was useful in more than half of the patients with GHD in adults, which confirms the literature data on the need to use it in the dynamics of monitoring patients in order to track and assess their quality of life in outpatient settings.

**Conclusions**

1) It was found that the frequency of GHD in adults in the examined patients with coronary heart disease of both groups was 15 cases out of 21 (71.4%). At the same time, in 8 (53.3%) patients with laboratory-determined GHD in adults, a reliable decrease in the concentration of IGF-1 in the blood plasma was noted.

2)Among the metabolic disorders in the examined patients, the following were encountered: obesity of 1-2 degrees – in 20 patients out of the total number of patients (95.2%), diabetes mellitus type 2 – in 7 (33.3%),

3) Using the questionnairefor the detection of AGHD (QoL AGHD) revealed a reliable decrease in scores in 15 (71.4%) patients during the preliminary survey. A reliable correlation between significantly reduced levels of GH, IGF-1 in blood plasma and a low score on the AGHD questionnaire was found in 8 patients of both groups - this is 38.0% of the total number of patients.

**References**

1. Dedov I.I., Peterkova V.A., Bezlepkina O.B./ National consensus "Use of growth hormone in adults and children". III All-Russian scientific and practical conference // "Actual problems of neuroendocrinology" Moscow, October 6-7, 2003

2. Camacho P., Gariba H., Sizemora G. / "Evidence-based endocrinology" - // Moscow, 2009, 632 p.

3.Shchukina. V.N./"The role of somatotropic insufficiency in the genesis of coronary heart disease in patients with type 2 diabetes mellitus" // - author, PhD. Moscow, 2006, 28 p. 183)

4.Urmanova Yu.M., Shakirova M.Yu., Rikhsieva N.T., Abduvakhabova M.B., Tursunkulov O.A."Complications of growth hormone deficiency in adults"//Journal of Theoretical and Clinical Medicine, 2018, No. 5, pp. 100-104

5.Urmanova Yu.M., Shakirova M.Yu., Rikhsieva N.T., Khodzhaeva F.S."Some risk factors for recurrence of inactive pituitary adenomas in patients with growth hormone

deficiency."// International Endocrinology Journal, Ukraine, Kyiv Shakhri, No. 2, Vol. 5, 2019, pp. 46-50
6.Attanavio A.F., D. Mo., E.M. Erfug.The frequency of Metabolic syndrome in patients with hypopituitarism and GHD before and after replacement therapy//J Clin Endoc and Met.-N1 95: 74-81, 2010
7.Grossman AB.Growth hormone deficiency in adults//London, Copyright 2005 by S. Karger AG, PO Box, CH-4009 Basel (Switzerland), Tom 33, 315 pages
8. JOL Jorgensen, JS Christiansen/GHD in adults//Denmark, Frontiers of Hormone research, editor AB Grossman, Vol.33, 2005, pg. 260
9.Johannson G, Bengtsson BA, Andersson B.Long term cardiovascular effects of GH treatment on cardiac structure. //Clin Endocrinol (Oxf) 1996;45:305-314.
10.Ken KY Ho /Consensus quidelines for the diagnosis and treatment of adults with GH-deficiency 11: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society , and Endocrine Society of Australia // European Journal of Endocrinology (2007) 157 – 695-700)
11. Syuzen M. Veb, Daogun Mo, Stiven B.Dg/Metabolic, cardio-vascular, and cerebro-vascular complications in patients with growth hormone deficiency and with Cushing disease or NFPA//Journ Clin End and Met., 2007, vol 95, N2, pg 201-210
12.Tomlinson J.KAssociation between premature mortality and hypopituitarism/et all//Lancet, .2001;357:425-431)
13.Ur E, Serri O, Legg K, Murphy LJ, Ezzat S /Canadian guidelines for the management of adult growth hormone deficiency.// Clin Invest Med. 2006 Apr;29(2):83-90.