FREQUENT ASSOCIATION OF VITILIGO WITH AUTOIMMUNE ENDOCRINE DISEASES: PRIMARY DATA OF THE RUSSIAN COHORT OF ADULT PATIENTS

Nuralieva NF[1] ✉, Yukina MYu[1], Troshina EA[1], Zhukova OV[2,3], Petrov VA[2], Volnukhin VA[2]

[1] Endocrinology Research Centre, Moscow, Russia

[2] Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology, Moscow, Russia

[3] Peoples' Friendship University of Russia, Moscow, Russia

There is evidence in the literature about more frequent association of vitiligo with autoimmune endocrine diseases (AEDs) compared to general population. No full-fledged studies aimed at assessing the prevalence of AEDs in the Russian cohort of adult vitiligo patients have been conducted. The study was aimed to assess the prevalence of AEDs in the cohort of Russian adult vitiligo patients. Patients with vitiligo monitored in two clinics, the Endocrinology Research Centre (Clinic 1; *n* = 39) and the Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology (Clinic 2; *n* = 26), were enrolled. Along with clinical examination, screening laboratory tests were performed in all patients in order to reveal AEDs. The majority of patients (more than 95% of cases) had nonsegmental vitiligo. Among patients monitored in Clinic 1, AEDs were diagnosed in 85% of cases: isolated AEDs accounted for 39%, while multiple AEDs were found in 46% of cases. Autoimmune thyroid diseases were diagnosed in 69% of cases. Autoimmune adrenal insufficiency was found in 28% of patients, type 1 diabetes mellitus in 21%, hypoparathyroidism in 13%, hypergonadotropic hypogonadism in 10%, endocrine ophthalmopathy in 10% of patients. Among patients monitored in Clinic 2, AEDs were diagnosed in four patients (15% of cases): three patients had primary hypothyroidism in the outcome of autoimmune thyroiditis, one patient had Graves' disease. Thus, the prevalence of AEDs in patients with vitiligo may vary between 15–85%. Vitiligo is most often associated with autoimmune thyroid diseases (15–69%). Vitiligo patients should undergo annual screening aimed at detection of autoimmune endocrine disorders, especially thyroid diseases.

Keywords: vitiligo, autoimmune thyroiditis, type 1 diabetes mellitus, Graves' disease, autoimmune adrenal insufficiency, autoimmune polyglandular syndrome, prevalence

Funding: this work was supported by Foundation for Scientific and Technological Development of Yugra (agreement No 2022-05-01/2022).

Author contribution: Nuralieva NF — endocrinology examination, data acquisition, statistical analysis, literature analysis, manuscript writing, preparation of the article for publication; Yukina MYu — study concept development, endocrinology examination, manuscript editing; Troshina EA — approval of the study concept and the final text of the manuscript; Zhukova OV — approval of the final text of the manuscript; Petrov VA — dermatology examination, data acquisition, literature analysis; Volnukhin VA — approval of the study concept, dermatology examination, manuscript editing and approval of the final text.

Compliance with ethical standards: the study was approved by the Ethics Commitee of the Endocrinology Research Centre (protocol № 17 of 27 September 2017); the informed consent was submitted by all patients.

✉ **Correspondence should be addressed:** Nurana F. Nuralieva
Dmitriya Ulyanova, 11, Moscow, 117292, Russia; nnurana@yandex.ru

Received: 29.09.2022 **Accepted:** 13.10.2022 **Published online:** 29.10.2022

DOI: 10.24075/brsmu.2022.055

ЧАСТАЯ АССОЦИАЦИЯ ВИТИЛИГО С ЭНДОКРИННЫМИ АУТОИММУННЫМИ ЗАБОЛЕВАНИЯМИ: ПЕРВИЧНЫЕ ДАННЫЕ В РОССИЙСКОЙ КОГОРТЕ ВЗРОСЛЫХ ПАЦИЕНТОВ

Н. Ф. Нуралиева[1] ✉, М. Ю. Юкина[1], Е. А. Трошина[1], О. В. Жукова[2,3], В. А. Петров[2], В. А. Волнухин[2]

[1] Национальный медицинский исследовательский центр эндокринологии, Москва, Россия

[2] Московский научно-практический центр дерматовенерологии и косметологии, Москва, Россия

[3] Российский университет дружбы народов, Москва, Россия

В литературе имеются данные о более частой, чем в популяции, ассоциации витилиго с эндокринными аутоиммунными заболеваниями (эАИЗ). В российской когорте полноценных исследований, направленных на оценку частоты встречаемости эАИЗ у взрослых пациентов с витилиго, не проводилось. Целью исследования было проанализировать частоту встречаемости эАИЗ в когорте российских взрослых пациентов с витилиго. В него вошли пациенты с витилиго, наблюдавшиеся в двух лечебных учреждениях: «НМИЦ эндокринологии» (центр 1; *n* = 39) и в «МНПЦДК ДЗМ» (центр 2; *n* = 26). Всем пациентам наряду с клиническим обследованием проводили скрининговое лабораторное обследование с целью выявления эАИЗ. У большинства пациентов (более 95% случаев) установлен несегементарный тип витилиго. Среди пациентов, наблюдавшихся в центре 1, эАИЗ диагностированы в 85% случаев: у 39% выявлено одно эАИЗ, у 46% — множественные эАИЗ. Аутоиммунные заболевания щитовидной железы встречались в 69% случаев. У 28% пациентов выявлена аутоиммунная надпочечниковая недостаточность, у 21% — сахарный диабет 1-го типа, у 13% — гипопаратиреоз, у 10% — гипергонадотропный гипогонадизм, у 10% — эндокринная офтальмопатия. Среди пациентов, наблюдавшихся в центре 2, эАИЗ диагностированы у четырех больных (15% случаев): у троих — выявлен первичный гипотиреоз в исходе в аутоиммунного тиреоидита, у одного — болезнь Грейвса. Таким образом, частота встречаемости эАИЗ у пациентов с витилиго может варьировать от 15 до 85%. Наиболее часто (15–69%) витилиго ассоциируется с аутоиммунными тиреопатиями. Пациентам с витилиго показано ежегодное скрининговое обследование с целью выявления аутоиммунной эндокринной патологии, особенно заболеваний щитовидной железы.

Ключевые слова: витилиго, аутоиммунный тиреоидит, сахарный диабет 1-го типа, болезнь Грейвса, аутоиммунная надпочечниковая недостаточность, аутоиммунный полигландулярный синдром, распространенность

Финансирование: работа поддержана Фондом научно-технологического развития Югры, Соглашение № 2022-05-01/2022.

Вклад авторов: Н. Ф. Нуралиева — эндокринологическое обследование, сбор материала, статистический анализ данных, анализ литературы, написание статьи; М. Ю. Юкина — концепция исследования, эндокринологическое обследование, редактирование статьи; Е. А. Трошина — утверждение концепции исследования, редактирование статьи; О. В. Жукова — редактирование статьи; В. А. Петров — дерматологическое обследование, сбор материала, анализ литературы; В. А. Волнухин — утверждение концепции исследования, дерматологическое обследование, редактирование статьи.

Соблюдение этических стандартов: исследование одобрено этическим комитетом ФГБУ «НМИЦ эндокринологии» (протокол № 17 от 27 сентября 2017 г.); все пациенты подписали добровольное информированное согласие на участие в исследовании.

✉ **Для корреспонденции:** Нурана Фейзуллаевна Нуралиева
ул. Дмитрия Ульянова, д. 11, г. Москва, 117292, Россия; nnurana@yandex.ru

Статья получена: 29.09.2022 **Статья принята к печати:** 13.10.2022 **Опубликована онлайн:** 29.10.2022

DOI: 10.24075/vrgmu.2022.055

Vitiligo is a common polygenic autoimmune disease characterized by formation of the foci of skin depigmentation, resulting from the death or decreased function of melanocytes, on various parts of the body. Segmental and nonsegmental vitiligo are distinguished. Segmental vitiligo is characterized by unilateral lesions located within one or more body segments. Nonsegmental vitiligo results in a few or multiple foci of depigmentation that are often symmetrically arranged [1]. In foreign literature, there is evidence of the higher incidence of autoimmune endocrine diseases (AEDs) in patients with vitiligo compared to the general population [1–3]. Autoimmune thyropathies are the most common in vitiligo patients (0.3–40% cases) [4–12]: autoimmune thyroiditis (AIT) is diagnosed in 0.3–31% of cases [9, 13, 14], and Graves' disease (GD) is found in 0.3–17.1% of cases [9, 14–16]; thyroid autoantibody positivity is identified in 41.8% of cases [11]. Type 1 diabetes mellitus (T1D) is found in vitiligo patients in 0.1–25% of cases [4, 5, 8–11, 17], autoimmune adrenal insufficiency (AAI) is diagnosed in 0.2–3.2% of cases [4, 5], and anti-adrenal antibodies are detected in 2.5% of cases [18, 19].

Vitiligo can not only be coupled with isolated AEDs, but also be a component of autoimmune polyglandular syndrome (APS), the primary autoimmune disorder that affects two or more peripheral endocrine glands and usually results in the endocrine gland dysfunction. APS type 1 (APS-1) and type 2 (APS-2) are distinguished. Candidiasis involving the skin and mucous membranes, hypoparathyroidism, and AAI are the main components of APS-1. Patients with APS-2 develop such main AEDs, as AAI, T1D, autoimmune thyropathies (GD or AIT), in combination with other autoimmune diseases [2]. Vitiligo often becomes the first component of APS (in 12.6% of cases [2]). APS can occur in 27.4% of vitiligo patients [1].

At the same time, high incidence of vitiligo development in patients with autoimmune endocrine diseases have been reported: it is found in 2.6–2.8% of patients with AIT [20, 21], 1.4–2.6% of patients with GD [20, 22], 23.3% of patients with T1D [23], 37% of patients with APS-1 [24], and 20% of patients with APS-2 [2].

Published research shows that autoimmune endocrine diseases occur mostly in patients with nonsegmental vitiligo [1, 6, 7]. No other factors contributing to the risk of AEDs in vitiligo patients have been identified. According to some reports, [1, 7, 8], the patients' gender and race, as well as vitiligo duration and activity, do not define the rate of AEDs manifestations. Meanwhile, other studies revealed more frequent association of vitiligo with AEDs in females [1, 4, 8, 9] and patients with larger skin lesions [4, 8]. Furthermore, higher prevalence of autoimmune thyropathies associated with the prolonged course of vitiligo and predominant involvement of the skin of the trunk was reported [8]. These data were not confirmed by papers reporting higher incidence of autoimmune thyroid disorders (AITDs) in patients with vitiligo patches located mostly on their limbs and joints [4], as well as predominance of APS in patients with acrofacial vitiligo [1]. The results of some studies suggest that the increased risk of AITD manifestation is associated with the late-onset vitiligo [10, 25]. However, association of vitiligo with GD is most common in young patients [14].

No full-fledged studies aimed at assessing the prevalence of AEDs in adult vitiligo patients and the prevalence of vitiligo in patients with AEDs in the Russian cohort have been conducted. Single studies on the issue were focused on assessing the incidence of vitiligo in patients with diabetes mellitus [26] or the AITD and pancreatic islet autoimmunity marker antibodies carrier state in vitiligo patients [27].

The study was aimed to assess the prevalence of AEDs in the cohort of Russian vitiligo patients.

METHODS

Patients included in the study

The first part of the study involved patients with vitiligo monitored in 2019–2021 in the Endocrinology Research Centre. The second part of the study involved patients with vitiligo monitored in 2019–2021 in the Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology.

The patients were recruited and allocated to certain groups based on their compliance with the inclusion criteria and non-compliance with the exclusion criteria.

Inclusion criteria: age 18 or older; vitiligo; availability of the patient's informed consent.

Exclusion criteria: pregnancy, lactation; acute infections; exacerbation of chronic diseases; severe life-threatening conditions; congenital or acquired immunodeficiency disorders; taking medications affecting the immune system function (glucocorticoids not for vital indications, interleukins, interferons, immunoglobulins, immunosuppressants, cytostatics), and/or vaccination/revaccination within a month prior to enrollment.

Study design: cross-sectional observational descriptive study; the first part involved 39, and the second part involved 26 subjects. Continuous sampling was used during the study.

Clinical assessment

Medical researchers examined all the subjects in order to clarify their compliance with the inclusion criteria or possible non-compliance with the exclusion criteria. Initial examination included patient complaint management and history taking, as well as measuring anthropometric parameters, blood pressure and pulse rate. Family history, acute and chronic diseases, taking medications and dietary supplements, harmful habits, and gynecologic history (in women) were specified.

Dermatovenerologist performed thorough visual examination of the patient that involved assessment of the skin and skin appendages, and photodocumentation of lesions under visible light or Wood's lamp using digital camera.

Laboratory tests

Screening laboratory tests for all the major AEDs were performed in all patients. Biochemical, immunological and hormonal tests were carried out in the clinical diagnostic laboratory at the Endocrinology Research Centre. Blood was collected from the cubital vein in the vacuum tubes containing inert gel and ethylenediaminetetraacetic acid in the morning (between 08:00 am and 10:00 am) in the fasting state (fasting for 8–14 hrs prior to venipuncture). The samples were centrifuged within 15 minutes after blood collection and processed. Complete blood count, biochemical, hormonal, and immunological (thyroid peroxidase (TPO) antibodies, thyroglobulin (TG) antibodies) tests were carried out on the day of blood sampling. Serum samples for further assessment of the levels of 21-hydroxylase antibodies and markers of pancreatic islet autoimmunity had to be temporarily frozen in microtubes at a temperature of –80 °C.

Statistical analysis of the results

Statistical processing of the results was performed by standard methods using the STATISTICA 13 software package (StatSoft; USA).

Table 1. Characteristics of study participants

Group	Patients				
	n	Age (years)	Gender (F/M)		
			n	%	ratio
Patients initially monitored in Clinic 1	39	19–73	26/13	67/33	2.0 : 1
Patients initially monitored in Clinic 2	26	19–71	17/9	65/35	1.9 : 1

Note: M — male, F — female.

Chi-squared test (χ^2) was used to compare qualitative traits. The differences were considered significant at $p < 0.05$.

RESULTS

Characteristics of study participants are provided in Table. 1.

The prevalence of autoimmune endocrine diseases in the cohort of adult patients with vitiligo initially monitored in the Endocrinology Research Centre

In the surveyed cohort, symptomatic AEDs were diagnosed in 85% of cases (*n* = 33). Single AED was diagnosed in 38.5% of cases (*n* = 15), and in 46.1% of cases (*n* = 18) multiple autoimmune endocrine disorders were observed. Another 6 patients (15.4%) with no symptomatic AEDs appeared to be carriers of AITD marker antibodies showing no target organ dysfunction and/or carriers of pancreatic islet autoimmunity marker antibodies showing no carbohydrate metabolism disorders.

AITDs were found in 69% of cases (*n* = 27): 19 patients (70%) were diagnosed with primary hypothyroidism in the outcome of AIT, 8 patients (30%) were diagnosed with GD. AAI was found in 28% of cases (*n* = 11), T1D/LADA (latent autoimmune diabetes in adults) in 21% (*n* = 8), hypoparathyroidism in 13% (*n* = 5), hypergonadotropic hypogonadism (HH) in 10% (*n* = 4), endocrine ophthalmopathy (EOP) in 10% of cases (*n* = 4).

Multiple autoimmune endocrine disorders were represented by APS-2 in 61% of cases (*n* = 11), APS-1 in 22% of cases (*n* = 4); a combination of GD and EOP was found in 17% of cases (*n* = 3). The onset of AEDs was preceded by vitiligo in 30% of patients (*n* = 10), 12% of patients developed vitiligo and AEDs simultaneously (*n* = 4).

The AITDs marker antibodies carrier state with no target organ dysfunction was found in 15% of cases (*n* = 6), while the pancreatic islet autoimmunity marker antibodies positivity with no carbohydrate metabolism disorder was diagnosed in 23% of cases (*n* = 9) (see Fig.). No carriers of 21-hydroxylase antibodies having no disorders of the adrenal cortex were found.

The patients were diagnosed with nonsegmental vitiligo in 100% of cases. However, one patient with APS-2 (AAI, primary hypothyroidism in the outcome of AIT, autoimmune gastritis) was diagnosed with universal vitiligo.

Comparison of the prevalence of AEDs in female and male patients is provided in Table 2.

The prevalence of autoimmune endocrine diseases in the cohort of adult patients with vitiligo initially monitored in the Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology

AEDs were diagnosed in four patients (15%). All the diagnosed AEDs were classified as AITDs. Among them primary hypothyroidism in the outcome of AIT was found in three patients, and Graves' disease was found in one patient.

AITDs marker antibodies positivity with no thyroid dysfunction was diagnosed in 15% of cases (*n* = 4).

Nonsegmental vitiligo was diagnosed in 25 patients (96%). One patient with no symptomatic AEDs or antibody positivity was diagnosed with segmental vitiligo.

Comparison of the prevalence of AEDs in female and male patients is provided in Table 3.

Table 2. The prevalence of AEDs and the AITDs and pancreatic islet autoimmunity marker antibodies positivity in female and male vitiligo patients initially monitored in the Endocrinology Research Centre

AEDs	F *n* = 26	M *n* = 13	*p*
AEDs, *n* (%)	23 (88)	10 (77)	0,347
AITDs, *n* (%)	19 (73)	8 (62)	0,462
Primary hypothyroidism in the outcome of AIT, *n* (%)	14 (54)	5 (39)	0,365
GD, *n* (%)	5 (19)	3 (23)	0,779
AAI, *n* (%)	11 (42)	0	**0,006**
T1D/LADA, *n* (%)	3 (12)	5 (39)	**0,0497**
Hypoparathyroidism, *n* (%)	4 (15)	1 (8)	0,498
HH, *n* (%)	4 (15)	0	0,136
EOP, *n* (%)	2 (8)	2 (15)	0,455
APS-1, *n* (%)	4 (15)	0	0,136
APS-2, *n* (%)	8 (31)	3 (23)	0,615
GD + EOP, *n* (%)	2 (8)	1 (8)	1
AITDs marker antibodies positivity with no target organ dysfunction, *n* (%)	5 (19)	1 (8)	0,347
Pancreatic islet autoimmunity marker antibodies positivity with no carbohydrate metabolism disorder, *n* (%)	5 (19)	4 (31)	0,42

Note: M — male, F — female.

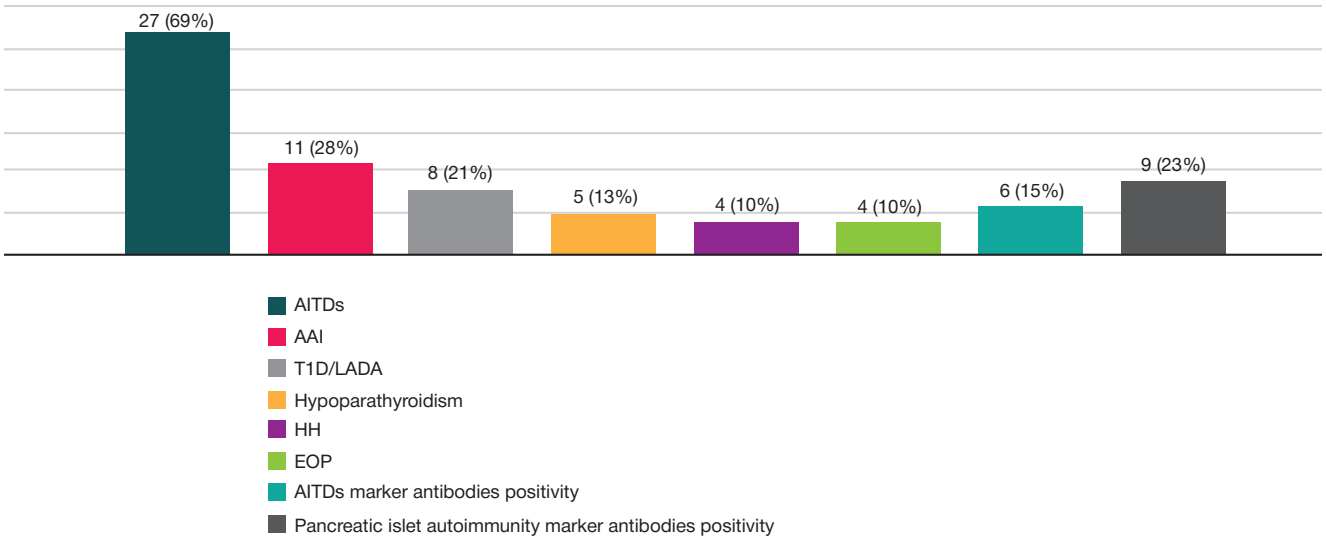

Fig. The prevalence of autoimmune endocrine disorders in the cohort of adult patient with vitiligo initially monitored in the Endocrinology Research Centre

DISCUSSION

Our data on the prevalence of AEDs in patients with vitiligo are consistent with the results of other studies [4, 10, 28]. However, there is a report about one patient with AED (GD) among 204 vitiligo patients [16]. Most probably such low prevalence of AEDs reported by this paper is due to research methods based on the medical history analysis, while we performed active laboratory screening for AEDs.

According to the results of both first and second parts of the study, vitiligo is most often associated with AITDs, which is comparable with the data obtained by other researchers [4, 5, 10, 11]. At the same time, the study that included 50 vitiligo patients [12] revealed no cases of symptomatic AITDs, however, the authors reported high prevalence of TPO antibodies positivity (50% of cases; our study showed that the prevalence of TPO and TG antibodies positivity with no thyroid dysfunction was much lower, 15%).

Unlike other authors [1, 4, 8–10, 26], we found no signficant predominance of women among patients with AEDs associated with vitiligo, including multiple AEDs (except AAI). At the same time, we found that association of vitiligo with T1D was more frequent in the cohort on men compared to women. However, it is necessary to take into account similar gender differences in the general population (higher prevalence of T1D in men [29] and AAI in women [30]).

Furthermore, our findings confirm some data [5] that vitiligo often precedes AEDs manifestation. The results obtained justify the need for regular screening of vitiligo patients for AEDs.

Nonsegmental vitiligo was found in all patients monitored in the Endocrinology Research Centre and 96% of patients monitored in the Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology. However, it must be noted that nonsegmental vitiligo was diagnosed in both patients with symptomatic AEDs or carriers of antibodies against target organs and patients with no symptomatic AEDs or target organ antibodies positivity. Since our findings do not allow an unambiguous conclusion about the risk of AEDs in patients with various types of vitiligo (due to small number of patients with segmental vitiligo), further accumulation of data is required.

CONCLUSIONS

According to our data, the prevalence of AEDs in patients with vitiligo may vary between 15–85%. Vitiligo is most often associated with AITDs. Vitiligo precedes AEDs manifestation in 30% of cases. Among patients with vitiligo and symptomatic endocrine disorders, AAI is most common in women, while T1D is most often found in men. Vitiligo patients should undergo annual screening aimed at detecting autoimmune endocrine disorders, especially of thyroid disease. In is necessary to inform physicians (primarily dermatologists, endocrinologists, and general practitioners) about the possible association of vitiligo with autoimmune endocrine disorders. Patients should be made aware of the need for annual screening and referral to endocrinologist in case of emergence of the AEDs clinical manifestations.

Table 3. The prevalence of AEDs and antibodies positivity in female and male vitiligo patients initially monitored in the Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology

AEDs	F *n* = 17	M *n* = 9	*p*
AEDs, *n* (%)	4 (24)	0	0.114
AITDs, *n* (%)	4 (24)	0	0.114
Primary hypothyroidism in the outcome of AT, *n* (%)	3 (18)	0	0.18
GD, *n* (%)	1 (6)	0	0.458
AITDs marker antibodies positivity with no target organ dysfunction, *n* (%)	1 (6)	3 (33)	0.065

Note: M — male, F — female.

References

1. Amerio P, Di Rollo D, Carbone A, Auriemma M, Marra ME, De Remigis P, et al. Polyglandular autoimmune diseases in a dermatological clinical setting: vitiligo-associated autoimmune diseases. Eur J Dermatol. 2010; 20 (3): 354–8. DOI: 10.1684/ejd.2009.0939.
2. Hansen MP, Matheis N, Kahaly GJ. Type 1 diabetes and polyglandular autoimmune syndrome: A review. World J Diabetes. 2015; 6 (1): 67–79. DOI: 10.4239/wjd.v6.i1.67.
3. Perheentupa J. Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy. J Clin Endocrinol Metab. 2006; 91 (8): 2843–50. DOI: 10.1210/jc.2005-2611.
4. Van Geel N, Speeckaert M, Brochez L, Lambert J, Speeckaert R. Clinical profile of generalized vitiligo patients with associated autoimmune/autoinflammatory diseases. J Eur Acad Dermatol Venereol. 2014; 28 (6): 741–6. DOI: 10.1111/jdv.12169.
5. Korkij W, Solatani K, Simjee S, Marcincin PG, Chuang TY. Tissue-specific autoantibodies and autoimmune disorders in vitiligo and alopecia areata: a retrospective study. J Cutan Pathol. 1984; 11 (6): 522–30. DOI: 10.1111/j.1600-0560.1984.tb00413.x.
6. Yuan J, Sun C, Jiang S, Lu Y, Zhang Y, Gao X-H, et al. The prevalence of thyroid disorders in patients with vitiligo: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2019; 9: 803. DOI: 10.3389/fendo.2018.00803.
7. Fan KC, Yang TH, Huang YC. Vitiligo and thyroid disease: a systematic review and meta-analysis. Eur J Dermatol. 2018; 28 (6): 750–63. DOI: 10.1684/ejd.2018.3449.
8. Gey A, Diallo A, Seneschal J, Léauté-Labrèze C, Boralevi F, Jouary T, et al. Autoimmune thyroid disease in vitiligo: multivariate analysis indicates intricate pathomechanisms. Br J Dermatol. 2013; 168 (4): 756–61. DOI: 10.1111/bjd.12166.
9. Chen Y, Chen Y, Hwang C, Lin MW, Chen TJ, Chen CC, et al. Comorbidity profiles in association with vitiligo: a nationwide population-based study in Taiwan. J Eur Acad Dermatol Venereol. 2015; 29 (7): 1362–9. DOI: 10.1111/jdv.12870.
10. Lazzeri L, Colucci R, Cammi A, Dragoni F, Moretti S. Adult onset vitiligo: multivariate analysis suggests the need for a thyroid screening. Biomed Res Int. 2016; 2016: 1–5. DOI: 10.1155/2016/8065765.
11. Ingordo V, Cazzaniga S, Raone B, Digiuseppe MD, Musumeci ML, Fai D, et al. Circulating Aautoantibodies and autoimmune comorbidities in vitiligo patients: a multicenter Italian study. Dermatology. 2014; 228 (3): 240–9. DOI: 10.1159/000357807.
12. Kumar K, Priya S, Sharma R, Kapoor U, Saini M, Bisht YS. Autoimmune thyroid disease in patients with vitiligo: prevalence study in India. Endocr Pract. 2012; 18 (2): 194–9. DOI: 10.4158/EP11205.OR.
13. Akay BN, Bozkir M, Anadolu Y, Gullu S. Epidemiology of vitiligo, associated autoimmune diseases and audiological abnormalities: Ankara study of 80 patients in Turkey. J Eur Acad Dermatol Venereol. 2010; 24 (10): 1144–50. DOI: 10.1111/j.1468-3083.2010.03605.x.
14. Bae J, Lee J, Yun J, Han B, Han TY. Vitiligo and overt thyroid diseases: A nationwide population-based study in Korea. J Am Acad Dermatol. 2017; 76 (5): 871–8. DOI: 10.1016/j.jaad.2016.12.034.
15. Hegedus L, Heidenheim M, Gervil M, Hjalgrim H, Høier-Madsen M. High frequency of thyroid dysfunction in patients with vitiligo. Acta Derm Venereol. 1994; 74 (2): 120–3. DOI: 10.2340/0001555574120123.
16. Poojary S. Vitiligo and associated autoimmune disorders: A retrospective hospital-based study in Mumbai, India. Allergol Immunopathol (Madr). 2011; 39 (6): 356–61. DOI: 10.1016/j.aller.2010.12.007.
17. Sivasubramanian A, Ganapathi S. The study on association of co-morbidities in female patients with vitiligo. Int J Res Dermatol. 2019; 5 (1): 203. DOI: 10.18203/issn.2455–4529.
18. Liu CW, Huang YC. Vitiligo and autoantibodies: a systematic review and meta-analysis. J Dtsch Dermatol Ges. 2018; 16 (7): 845–51. DOI: 10.1111/ddg.13574.
19. Laberge G, Mailloux C, Gowan K, Holland P, Bennett DC, Fain PR, et al. Early disease onset and increased risk of other autoimmune diseases in familial generalized vitiligo. Pigment Cell Res. 2005; 18 (4): 300–5. DOI: 10.1111/j.1600-0749.2005.00242.x.
20. Boelaert K, Newby PR, Simmonds MJ, Holder RL, Carr-Smith JD, Heward JM, et al. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med. 2010; 123 (2): 183.e1–9. DOI:10.1016/j.amjmed.2009.06.030.
21. Ruggeri R, Trimarchi F, Giuffrida G, Certo R, Cama E, Campennì A, et al. Autoimmune comorbidities in Hashimoto's thyroiditis: different patterns of association in adulthood and childhood/adolescence. Eur J Endocrinol. 2017; 176 (2): 133–41. DOI: 10.1530/EJE-16-0737.
22. Ferrari S, Fallahi P, Ruffilli I, Elia G, Ragusa F, Benvenga S, et al. The association of other autoimmune diseases in patients with Graves' disease (with or without ophthalmopathy): Review of the literature and report of a large series. Autoimmun Rev. 2019; 18 (3): 287–92. DOI: 10.1016/j.autrev.2018.10.001.
23. Nederstigt C, Uitbeijerse B, Janssen L, Corssmit EPM, de Koning EJP, Dekkers OM. Associated autoimmune disease in type 1 diabetes patients: a systematic review and meta-analysis. Eur J Endocrinol. 2019; 180 (2): 135–44. DOI: 10.1530/EJE-18-0515.
24. Ferre E, Rose S, Rosenzweig S, Burbelo PD, Romito KR, Niemela JE, et al. Redefined clinical features and diagnostic criteria in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy. JCI Insight. 2016; 1 (13): e88782. DOI: 10.1172/jci.insight.88782.
25. Nicolaidou E, Antoniou C, Miniati A, Lagogianni E, Matekovits A, Stratigos A, et al. Childhood- and later-onset vitiligo have diverse epidemiologic and clinical characteristics. J Am Acad Dermatol. 2012; 66 (6): 954–8. DOI: 10.1016/j.jaad.2011.07.010.
26. Turiev GS. Autoimmunnye zabolevaniya u bol'nyx saxarnym diabetom vzroslyx. Vladikavkazskij mediko-biologich. vestn. 2013; 17 (26): 74–80. Russian.
27. Lomonosov KM, Simonova NI, Lomonosov MK. Sravnitel'nyj analiz syvorotochnogo soderzhaniya autoantitel u bol'nyx vitiligo. Ros. zhurn. kozhnyx i venericheskix boleznej. 2013; 2: 35. Russian.
28. Agarwala S, Malkud S. A study on the clinico-epidemiological profile of vitiligo patients and its association with endocrine, audiological and ocular abnormalities. Iran J Dermatol. 2020; 23: 155–162. DOI: 10.22034/ijd.2020.120835.
29. Carstensen B, Rønn PF, Jørgensen ME. Prevalence, incidence and mortality of type 1 and type 2 diabetes in Denmark 1996–2016. BMJ Open Diabetes Res Care. 2020; 8 (1): e001071. DOI: 10.1136/bmjdrc-2019-001071.
30. Betterle C, Dal Pra C, Mantero F, Zanchetta R. Autoimmune adrenal insufficiency and autoimmune polyendocrine syndromes: Autoantibodies, autoantigens, and their applicability in diagnosis and disease prediction. Endocr Rev. 2002; 23 (3): 327–364. DOI: 10.1210/er.23.3.327.

Литература

1. Amerio P, Di Rollo D, Carbone A, Auriemma M, Marra ME, De Remigis P, et al. Polyglandular autoimmune diseases in a dermatological clinical setting: vitiligo-associated autoimmune diseases. Eur J Dermatol. 2010; 20 (3): 354–8. DOI: 10.1684/ejd.2009.0939.
2. Hansen MP, Matheis N, Kahaly GJ. Type 1 diabetes and polyglandular autoimmune syndrome: A review. World J Diabetes. 2015; 6 (1): 67–79. DOI: 10.4239/wjd.v6.i1.67.
3. Perheentupa J. Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy. J Clin Endocrinol Metab. 2006; 91 (8): 2843–50. DOI: 10.1210/jc.2005-2611.
4. Van Geel N, Speeckaert M, Brochez L, Lambert J, Speeckaert R. Clinical profile of generalized vitiligo patients with associated autoimmune/autoinflammatory diseases. J Eur Acad Dermatol

Venereol. 2014; 28 (6): 741–6. DOI: 10.1111/jdv.12169.
5. Korkij W, Solatani K, Simjee S, Marcincin PG, Chuang TY. Tissue-specific autoantibodies and autoimmune disorders in vitiligo and alopecia areata: a retrospective study. J Cutan Pathol. 1984; 11 (6): 522–30. DOI: 10.1111/j.1600-0560.1984.tb00413.x.
6. Yuan J, Sun C, Jiang S, Lu Y, Zhang Y, Gao X-H, et al. The prevalence of thyroid disorders in patients with vitiligo: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2019; 9: 803. DOI: 10.3389/fendo.2018.00803.
7. Fan KC, Yang TH, Huang YC. Vitiligo and thyroid disease: a systematic review and meta-analysis. Eur J Dermatol. 2018; 28 (6): 750–63. DOI: 10.1684/ejd.2018.3449.
8. Gey A, Diallo A, Seneschal J, Léauté-Labrèze C, Boralevi F, Jouary T, et al. Autoimmune thyroid disease in vitiligo: multivariate analysis indicates intricate pathomechanisms. Br J Dermatol. 2013; 168 (4): 756–61. DOI: 10.1111/bjd.12166.
9. Chen Y, Chen Y, Hwang C, Lin MW, Chen TJ, Chen CC, et al. Comorbidity profiles in association with vitiligo: a nationwide population-based study in Taiwan. J Eur Acad Dermatol Venereol. 2015; 29 (7): 1362–9. DOI: 10.1111/jdv.12870.
10. Lazzeri L, Colucci R, Cammi A, Dragoni F, Moretti S. Adult onset vitiligo: multivariate analysis suggests the need for a thyroid screening. Biomed Res Int. 2016; 2016: 1–5. DOI: 10.1155/2016/8065765.
11. Ingordo V, Cazzaniga S, Raone B, Digiuseppe MD, Musumeci ML, Fai D, et al. Circulating Aautoantibodies and autoimmune comorbidities in vitiligo patients: a multicenter Italian study. Dermatology. 2014; 228 (3): 240–9. DOI: 10.1159/000357807.
12. Kumar K, Priya S, Sharma R, Kapoor U, Saini M, Bisht YS. Autoimmune thyroid disease in patients with vitiligo: prevalence study in India. Endocr Pract. 2012; 18 (2): 194–9. DOI: 10.4158/EP11205.OR.
13. Akay BN, Bozkir M, Anadolu Y, Gullu S. Epidemiology of vitiligo, associated autoimmune diseases and audiological abnormalities: Ankara study of 80 patients in Turkey. J Eur Acad Dermatol Venereol. 2010; 24 (10): 1144–50. DOI: 10.1111/j.1468-3083.2010.03605.x.
14. Bae J, Lee J, Yun J, Han B, Han TY. Vitiligo and overt thyroid diseases: A nationwide population-based study in Korea. J Am Acad Dermatol. 2017; 76 (5): 871–8. DOI: 10.1016/j.jaad.2016.12.034.
15. Hegedus L, Heidenheim M, Gervil M, Hjalgrim H, Høier-Madsen M. High frequency of thyroid dysfunction in patients with vitiligo. Acta Derm Venereol. 1994; 74 (2): 120–3. DOI: 10.2340/0001555574120123.
16. Poojary S. Vitiligo and associated autoimmune disorders: A retrospective hospital-based study in Mumbai, India. Allergol Immunopathol (Madr). 2011; 39 (6): 356–61. DOI: 10.1016/j.aller.2010.12.007.
17. Sivasubramanian A, Ganapathi S. The study on association of co-morbidities in female patients with vitiligo. Int J Res Dermatol. 2019; 5 (1): 203. DOI: 10.18203/issn.2455–4529.
18. Liu CW, Huang YC. Vitiligo and autoantibodies: a systematic review and meta-analysis. J Dtsch Dermatol Ges. 2018; 16 (7): 845–51. DOI: 10.1111/ddg.13574.
19. Laberge G, Mailloux C, Gowan K, Holland P, Bennett DC, Fain PR, et al. Early disease onset and increased risk of other autoimmune diseases in familial generalized vitiligo. Pigment Cell Res. 2005; 18 (4): 300–5. DOI: 10.1111/j.1600-0749.2005.00242.x.
20. Boelaert K, Newby PR, Simmonds MJ, Holder RL, Carr-Smith JD, Heward JM, et al. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med. 2010; 123 (2): 183.e1–9. DOI:10.1016/j.amjmed.2009.06.030.
21. Ruggeri R, Trimarchi F, Giuffrida G, Certo R, Cama E, Campennì A, et al. Autoimmune comorbidities in Hashimoto's thyroiditis: different patterns of association in adulthood and childhood/adolescence. Eur J Endocrinol. 2017; 176 (2): 133–41. DOI: 10.1530/EJE-16-0737.
22. Ferrari S, Fallahi P, Ruffilli I, Elia G, Ragusa F, Benvenga S, et al. The association of other autoimmune diseases in patients with Graves' disease (with or without ophthalmopathy): Review of the literature and report of a large series. Autoimmun Rev. 2019; 18 (3): 287–92. DOI: 10.1016/j.autrev.2018.10.001.
23. Nederstigt C, Uitbeijerse B, Janssen L, Corssmit EPM, de Koning EJP, Dekkers OM. Associated autoimmune disease in type 1 diabetes patients: a systematic review and meta-analysis. Eur J Endocrinol. 2019; 180 (2): 135–44. DOI: 10.1530/EJE-18-0515.
24. Ferre E, Rose S, Rosenzweig S, Burbelo PD, Romito KR, Niemela JE, et al. Redefined clinical features and diagnostic criteria in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy. JCI Insight. 2016; 1 (13): e88782. DOI: 10.1172/jci.insight.88782.
25. Nicolaidou E, Antoniou C, Miniati A, Lagogianni E, Matekovits A, Stratigos A, et al. Childhood- and later-onset vitiligo have diverse epidemiologic and clinical characteristics. J Am Acad Dermatol. 2012; 66 (6): 954–8. DOI: 10.1016/j.jaad.2011.07.010.
26. Туриев Г. С. Аутоиммунные заболевания у больных сахарным диабетом взрослых. Владикавказский медико-биологич. вестн. 2013; 17 (26): 74–80.
27. Ломоносов К. М., Симонова Н. И., Ломоносов М. К. Сравнительный анализ сывороточного содержания аутоантител у больных витилиго. Рос. журн. кожных и венерических болезней. 2013; 2: 35.
28. Agarwala S, Malkud S. A study on the clinico-epidemiological profile of vitiligo patients and its association with endocrine, audiological and ocular abnormalities. Iran J Dermatol. 2020; 23: 155–162. DOI: 10.22034/ijd.2020.120835.
29. Carstensen B, Rønn PF, Jørgensen ME. Prevalence, incidence and mortality of type 1 and type 2 diabetes in Denmark 1996–2016. BMJ Open Diabetes Res Care. 2020; 8 (1): e001071. DOI: 10.1136/bmjdrc-2019-001071.
30. Betterle C, Dal Pra C, Mantero F, Zanchetta R. Autoimmune adrenal insufficiency and autoimmune polyendocrine syndromes: Autoantibodies, autoantigens, and their applicability in diagnosis and disease prediction. Endocr Rev. 2002; 23 (3): 327–364. DOI: 10.1210/er.23.3.327.