type of CTLA-4 gene than AG- and GG-genotype by 28.21% and 56.41% (c^2=27.92; p<0.001) and 15.39% and 46.16% (c^2=12.92; p<0.001), respectively, as well as the II degree of the thyroid gland enlargement – by 31,54% and 23,85% (c^2=7,02; p=0,03) (tab. 6). On the other hand, the II degree hyperplasia was more frequently diagnosed in the individuals with *AG*-genotype, than in those with *AA* – by 40.0% (c^2=9.60; p=0.002), as well as more frequently than I and III degree thyroid hyperplasia by 36.67% and 31.54% (c^2=10.06; p=0.007).

In patients with euthyroid goiter I degree of thyroid hyperplasia was more common: in those with wild A-allele of BCL-2 gene by 11,49-52,45% (r≤0,029-0,001), A-allele of CTLA-4 gene – by 25.86-35.35% (c^2=10.14-11.58; p=0.003-0.006), and favorable GG-genotype of the *Fas* gene by 46.43% and 60.03% (c^2=25.39; p<0.001) (tab. 7).

Patients with subclinical hypothyroidism were more often diagnosed with the II degree hyperplasia of the thyroid gland: in the carriers of intermediate genotype (AG) of BCL-2 gene and CTLA-4 gene, by 25.53% and 37.78% (r≤0.001) (tab. 7-8) and in the owners of favorable GG-genotype of Fas gene by 25.53% and 26.51% (c^2=11.33; p=0.003) (tab. 8).

TABLE 3. *The distribution of polymorphic variants of the BCL-2 (rs17759659), CTLA-4 (rs231775) and APO-1 / Fas (rs2234767) genes in patients with nodular forms of goiter against the background of autoimmune thyroiditis, considering the thyroid function*

The genes under study, n (%)		Control, n=25 (%)	The thyroid gland function, n (%)			c^2 p
			Euthyroid goiter, n=21	Subclinical hypothyroidism, n=58	Clinical hypothyroidism, n=16	
BCL-2 (A/G), n (%)	*AA*	3 (12.0)	4 (19.05)	3 (5.17)	2 (12.50)	c^2=3.67 p>0.05
	GA	21 (84.0)	16 (76.19)	53 (91.38)	12 (75.0)	c^2=4.44 p>0.05
	GG	1 (4.0)	1 (4.76)	2 (3.45)	2 (12.50)	c^2=2.11 p>0.05
c^2 p		c^2=64.80 p<0.001	c^2=27.0 p<0.001	c^2=131.9 p<0.001	c^2=18.75 p<0.001	–
CTLA-4 (+49G/A), n (%)	*AA*	15 (60.0)	10 (47.62)	28 (48.28)	9 (56.25)	c^2<1.0 p>0.05
	AG	9 (36.0)	10 (47.62)	27 (46.55)	7 (43.75)	c^2<1.0 p>0.05
	GG	1 (4.0)	1 (4.76)	3 (5.17)	0	c^2<1.0 p>0.05
c^2 p		c^2=36.48 p<0.001	c^2=11.57 p=0.003	c^2=31.09 p<0.001	c^2<1.0 p>0.05	–
Fas (-1377G/A), n (%)	*GA*	6 (24.0)	4 (19.05)	13 (22.41)	1 (6.25)	c^2=2.13 p>0.05
	GG	19 (76.0)	17 (80.95)	45 (77.59)	15 (93.75)	
c^2 p		c^2=72.20 p<0.001	c^2=16.10 p<0.001	c^2=35.31 p<0.001	c^2=24.50 p<0.001	–

TABLE 4. *The distribution of polymorphic variants of the BCL-2 (rs17759659), CTLA-4 (rs231775) and APO-1 / Fas (rs2234767) genes in patients with thyroid disorders, taking into account the degree of its enlargement*

The genes under study, n (%)		Control, n=25 (%)	The thyroid gland hyperplasia, n (%)			c^2 p
			I degree, n=59	II degree, n=40	III degree, n=26	
BCL-2 (A/G), n (%)	*AA*	3 (12.0)	5 (8.47)	1 (2.50)	4 (15.38)	c^2=3.59 p>0.05
	GA	21 (84.0)	52 (88.14)	38 (95.0)	20 (76.92)	c^2=3.59 p>0.05
	GG	1 (4.0)	2 (3.39)	1 (2.50)	2 (7.69)	c^2=1.21 p>0.05
c^2 p		c^2=64.80 p<0.001	c^2=119.9 p<0.001	c^2=102.7 p<0.001	c^2=33.69 p<0.001	–
CTLA-4 (+49G/A), n (%)	*AA*	15 (60.0)	34 (57.63)	11 (27.50)	14 (53.85)	c^2=9.26 p=0.01
	AG	9 (36.0)	23 (38.98)	29 (72.50)	10 (38.46)	c^2=12.34 p=0.002
	GG	1 (4.0)	2 (3.39)	0	2 (7.69)	p>0.05
c^2 p		c^2=36.48 p<0.001	c^2=40.32 p<0.001	c^2=16.20 p<0.001	c^2=12.92 p=0.002	–
Fas (-1377G/A), n (%)	*GA*	6 (24.0)	9 (15.25)	10 (25.0)	4 (15.38)	c^2=1,71 p>0,05
	GG	19 (76.0)	50 (84.75)	30 (75.0)	22 (84.62)	
c^2 p		c^2=72.20 p<0.001	c^2=56.98 p<0.001	c^2=20.0 p<0.001	c^2=24.92 p<0.001	–

TABLE 5. *The distribution of polymorphic variants of the BCL-2 (rs17759659), CTLA-4 (rs231775) and APO-1 / Fas (rs2234767) genes in patients with adenoma of the thyroid gland, considering the degree of its enlargement*

The genes under study, n (%)		Control, n=25 (%)	The thyroid gland hyperplasia, n (%)		c^2 p
			I degree, n=20	II degree, n=10	
BCL-2 (A/G), n (%)	*AA*	3 (12.0)	1 (5.0)	0	-
	GA	21 (84.0)	19 (95.0)	10 (100.0)	p>0.05
	GG	1 (4.0)	0	0	0
c^2 p		c^2=64.80 p<0.001	–	–	–
CTLA-4 (+49G/A), n (%)	*AA*	15 (60.0)	10 (50.0)	2 (20.0)	c^2<1,0 p>0,05
	AG	9 (36.0)	10 (50.0)	8 (80.0)	
	GG	1 (4.0)	0	0	–
c^2 p		c^2=36.48 p<0.001	–	c^2=7.20 p=0.007	–
Fas (-1377G/A*)*, n (%)	*GA*	6 (24.0)	4 (20.0)	1 (10.0)	c^2<1,0 p>0,05
	GG	19 (76.0)	16 (80.0)	9 (90.0)	
c^2 p		c^2=72.20 p<0.001	c^2=14.40 p<0.001	c^2=12.80 p<0.001	–

TABLE 6. *The distribution of polymorphic variants of the BCL-2 (rs17759659), CTLA-4 (rs231775) and APO-1 / Fas (rs2234767) genes in patients with nodular form of goiter against the background of autoimmune thyroiditis depending on the degree of the thyroid gland hyperplasia*

The genes under study, n (%)		Control, n=25 (%)	The thyroid gland hyperplasia, n (%)			c^2 p
			I degree , n=39	II degree, n=30	III degree, n=26	
BCL-2 (A/G), n (%)	*AA*	3 (12.0)	4 (10.26)	1 (3.33)	4 (15.38)	c^2=2.41 p>0.05
	GA	21 (84.0)	33 (84.62)	28 (93.33)	20 (76.92)	c^2=3.01 p>0.05
	GG	1 (4.0)	2 (5.13)	1 (3.33)	2 (7.69)	c^2<1.0 p>0.05
c^2 p		c^2=64,80 p<0,001	c^2=69.46 p<0.001	c^2=72.90 p<0.001	c^2=33.69 p<0.001	-
CTLA-4 (+49G/A), n (%)	*AA*	15 (60.0)	24 (61.54)	9 (30.0)	14 (53.85)	c^2=7.02 p=0.03
	AG	9 (36.0)	13 (33.33)	21 (70.0)	10 (38.46)	c^2=10.06 p=0.007
	GG	1 (4.0)	2 (5.13)	0	2 (7.69)	p>0.05
c^2 p		c^2=36,48 p<0,001	c^2=27.92 p<0.001	c^2=9.60 p=0.002	c^2=12.92 p=0.002	–
Fas (-1377G/A*)*, n (%)	*GA*	6 (24.0)	5 (12.82)	9 (30.0)	4 (15.38)	c^2=3.55 p>0.05
	GG	19 (76.0)	34 (87.18)	21 (70.0)	22 (84.62)	
c^2 p		c^2 =72,20 p<0,001	c^2 =43.13 p<0.001	c^2 =9.60 p=0.002	c^2=24.92 p<0.001	–

TABLE 7. *Association of polymorphic variants of the BCL-2 (rs17759659) gene with the degree of the thyroid gland hyperplasia and its function*

The genes under study, n (%)			The thyroid gland function, n (%)			c^2 p
			Euthyroid goiter, n=31	Subclinical hypothyroidism, n=71	Clinical hypothyroidism, n=23	
BCL-2 (A/G), n (%)	*AA*, n=10	I degree, n=5	4 (12.90)	1 (1.41)	0	p=0.029
		II degree, n=1	0	1 (1.41)	0	–
		III degree, n=4	0	2 (2.82)	2 (8.70)	p>0.05
	GA, n=110	I degree, n=52	23 (74.19)	24 (33.80)	5 (21.74)	c^2=19.07 p<0.001
		II degree, n=38	3 (9.68)	33 (46.48)	2 (8.70)	c^2=20.09 p<0.001
		III degree, n=20	0	8 (11.27)	12 (52.17)	p<0.001
	GG, n=5	I degree, n=2	1 (3.22)	1 (1.41)	0	p>0.05
		II degree, n=1	0	1 (1.41)	0	–
		III degree, n=2	0	0	2 (8.70)	–

The patients with clinical hypothyroidism were more often recorded with the third degree hyperplasia of the thyroid gland, including those with predominant heterozygous AG-genotype of BCL-2 and CTLA-4 genes by 40.90% (p<0.001) and 26.21% (p=0.002), respectively; GG-genotype of Fas gene – by 55.36% (c^2=29.70; p<0.001) (tab. 7-8).

TABLE 8. *Association of polymorphic variants of the CTLA-4 (rs231775) and APO-1 / Fas (rs2234767) genes with the degree of the thyroid gland hyperplasia and its function*

The genes under study, n (%)			The thyroid gland function, n (%)			c^2 p
			Euthyroid goiter, n=31 (%)	Subclinical hypothyroidism, n=71 (%)	Clinical hypothyroidism, n=23 (%)	
CTLA-4 (+49G/A), n (%)	*AA*, n=59	I degree, n=34	15 (48.39)	16 (22.53)	3 (13.04)	c^2=10.14 p=0.006
		II degree, n=11	0	10 (14.08)	1 (4.35)	p>0.05
		III degree, n=14	0	5 (7.04)	9 (39.13)	p<0.001
	AG, n=62	I degree, n=23	12 (38.71)	9 (12.68)	2 (8.70)	c^2=11.58 p=0.003
		II degree, n=29	3 (9.68)	25 (35.21)	1 (4.35)	c^2=13.52 p=0.001
		III degree, n=10	0	3 (4.22)	7 (30.43)	p=0.002
	GG, n=4	I degree, n=2	1 (3.22)	1 (1.41)	0	p>0.05
		II degree, n=0	0	0	0	–
		III degree, n=2	0	2 (2.82)	0	–
Fas (-1377 G/A), n (%)	*GA*, n=23	I degree, n=9	4 (12.90)	4 (5.63)	1 (4.35)	c^2=2.06 p>0.05
		II degree, n=10	0	10 (14.08)	0	–
		III degree, n=4	0	3 (4.22)	1 (4.35)	p>0.05
	GG, n=102	I degree, n=50	24 (77.42)	22 (30.99)	4 (17.39)	c^2=25.39 p<0.001
		II degree, n=30	3 (9.68)	25 (35.21)	2 (8.70)	c^2=11.33 p=0.003
		III degree, n=22	0	7 (9.86)	15 (65.22)	c^2=29.70 p<0.001

CONCLUSIONS

TA and NGAIT are more common in the carriers of the minor G-allele (GA- and GG-genotypes) of the *BCL*-2 gene and in homozygous ones having the main G allele (GG-genotype) of the *Fas* gene by 11.5 and 4.34 times (p<0.001), with no significant interdependence between the genotypes of the *CTLA*4 gene. We did not find any difference between the relative incidences of the genotypes of the analyzed genes in the patients with NGAIT and those with TA or depending on the TG function (euthyroid goiter, subclinical and clinical hypothyroidism). Hyperplasia of the TG in the patients in general as well as in those with NGAIT is associated with the wild A-alleles of the *CTLA*-4 gene (*AA*- and *AG*-genotypes): the I and III degree hyperplasia occurred reliably more frequently in carriers of the AA genotype by 30.13% and 26.35% (c^2=9.26; p=0.01), and II degree of the TG enlargement in the patients with AG genotype by 33.52% and 34.04% (c^2=12.34; p=0.002), respectively. In patients with NGAIT or TA, the TG function is associated with its hyperplasia and with polymorphic sites of the genes under study. In patients with euthyroid goiter the I degree thyroid hyperplasia is more common: by 11.49-52.45% (p≤0.029-0.001) in the carriers of the wild *A*-allele of the *BCL*-2 gene and by 11.49-52.45% (p≤0.029-0.001) in those with *A*-allele of the *CTLA*-4 gene and by 46.43% and 60.03% (p<0.001) with favorable GG-genotype of the *Fas* gene. In patients with clinical hypothyroidism, the III degree thyroid hyperplasia is more common: the carriers of the heterozygous *AG*-genotypes of the *BCL*-2 and *CTLA*-4 genes prevail by 40.90% (p<0.001) and 26.21% (p=0.002) respectively, and *GG*-genotype of the *Fas* gene by 55.36% (p<0.001).

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