

EVALUATION OF AUTOIMMUNE STATUS IN PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA

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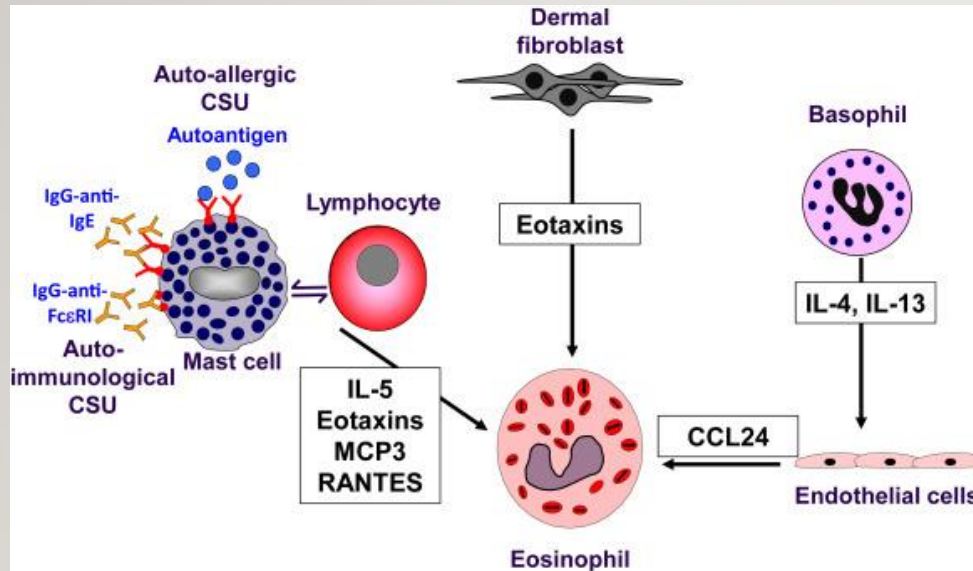
CHRONIC SPONTANEOUS URTICARIA (CSU)

- Chronic spontaneous (idiopathic) urticaria (CSU) is defined as the occurrence of wheals, angioedema, or both for more than 6 weeks
- affects 1–2% of the population
- CSU represents an important burden that compromises patient's quality of life, interferes with routine daily activities
- Autoimmunity (ie, autoimmune mechanisms of skin mast cell activation) is held to be a frequent underlying cause of CSU



Confino-Cohen R, Chodick G, Shalev V, Leshno M, Kimhi O, Goldberg A. Chronic urticaria and autoimmunity: associations found in a large population study. *J Allergy Clin Immunol.* 2012 May;129(5):1307-13. doi: 10.1016/j.jaci.2012.01.043. Epub 2012 Feb 14. PMID: 22336078.

PATHOGENESIS OF CSU



Kaplan AP. Chronic urticaria: pathogenesis and treatment. *J Allergy Clin Immunol.* 2004 Sep;114(3):465-74; quiz 475. doi: 10.1016/j.jaci.2004.02.049. PMID: 15356542

Key cells involved in CSU pathogenesis:

- Mast cells, basophils, eosinophils, lymphocytes, and neutrophils,
- Cytokines,
- Coagulation pathways and
- Autoantibodies (AABs)

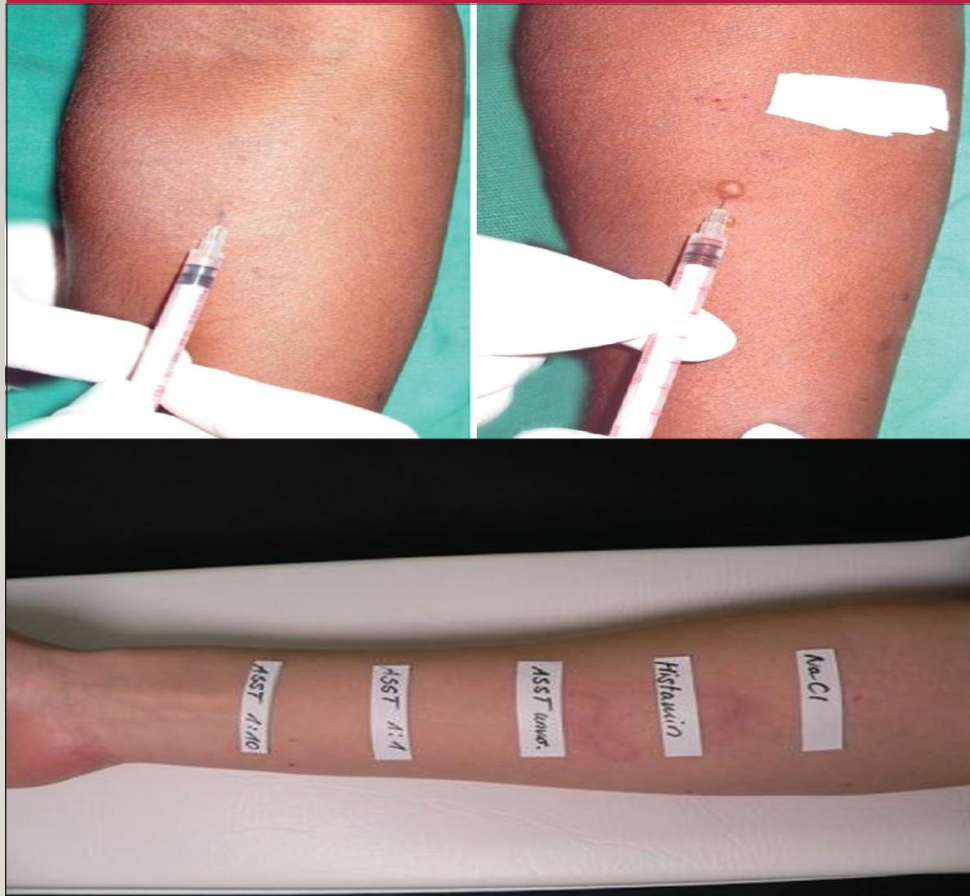
OBJECTIVE TO THIS STUDY

To investigate possible correlations between clinical and biological markers in patients with CSU and their associations with autoimmunity.

MATERIALS AND METHODS

- This prospective study was conducted from November 2020 to December 2021 in the department of Dermatology of the City General Hospital “ 8-mi Septemvri”, Skopje
- This study assessed 230 patients with CSU and 130 healthy subjects.
- **Autoimmune status** was inferred in the case of a personal history of concomitant autoimmune disease or in the presence of at least one type of AAbs (Autoantibodies): anti- thyroid peroxidase (Anti-TPO), anti-nuclear antibodies (ANA) and rheumatoid factor (RF). Broad clinical and biological analysis were performed.
- ASST was performed (intradermal injection of patients own serum on the forearm)

MATERIALS AND METHODS: ASST



- A positive test was defined as the appearance, within 30 minutes, of a red wheal with a diameter of 1.5 mm or greater than the wheal produced by the injection of normal saline solution.
- Patients were classified as either having a positive or a negative ASST.

Fagiolo U, Kricek F, Ruf C, Peserico A, Amadori A, Cancian M. Effects of complement inactivation and IgG depletion on skin reactivity to autologous serum in chronic idiopathic urticaria. *J Allergy Clin Immunol.* 2000 Sep;106(3):567-72. doi: 10.1067/mai.2000.108913. PMID: 10984379.

STATISTICAL ANALYSES

- Standard deviation (SD) with minimum and maximum values in brackets
- The Pearson's χ^2 test
- Mann-Whitney test and Kruskal-Wallis
- Wilcoxon- on matched-pairs signed rank test

RESULTS

PERSONAL HISTORY OF ATOPY AND AUTOIMMUNE DISEASES IN PATIENTS WITH CSU

Варијабла / Variable	n	ХСУ/ CSU n(%)
Лична историја за атопија/ Personal history of atopy		
Присуство/ present	145	145 (63.04)
без присуство/ not present	215	85 (36.96)
Лична историја за аутоимуна болест/ Personal history of autoimmune disease		
без присуство/ not present	242	112 (48.7)
Hashimoto Tireoiditis	66	66 (28.7)
Vitiligo	20	20 (8.7)
Arthritis Rheumatica	14	14 (6.09)
Morbus Crohn	8	8 (3.48)
Hashimoto Tireoiditis + Vitiligo	10	10 (4.35)

Present autoimmune diseases (51.3%):

- *Hashimoto Tireoiditis (28.7%),*
- *Vitiligo (8.7%),*
- *Arthritis Rheumatica (6.09%),*
- *Morbus Crohn (3.48%),*
- *Hashimoto Tireoiditis и Vitiligo (4.35%).*

RESULTS

PRESECEANCE OF AABS (AUTOANTIBODIES) IN CSU AND CG

Варијабла/ Variable	Група/ group			p-level
	n	ХСУ/CSU	КГ/CG	
Anti TPO (U/ml)				
mean ±SD	344.7± 465.0		27.7 ± 17.3	Z=8.5 *p=0.000000
median (IQR)	45 (32 – 780)		26 (12 – 44)	
0 – 60	n (%)	279	149 (64.78)	X ² =5907 *p=0.000000
>60	n (%)	81	81 (35.22)	
RF (IU/ml)				
mean ±SD	9.2± 14.8		7.8± 3.7	Z=4.9 *p=0.000001
median (IQR)	7 (5 – 11)		5 (3 – 8)	
0 – 15.9	n (%)	338	208 (90.43)	X ² =13.2 *p=0.00027
>15.9	n (%)	22	22 (9.57)	

Presecence of AAbs (Autoantibodies) in CSU patients:

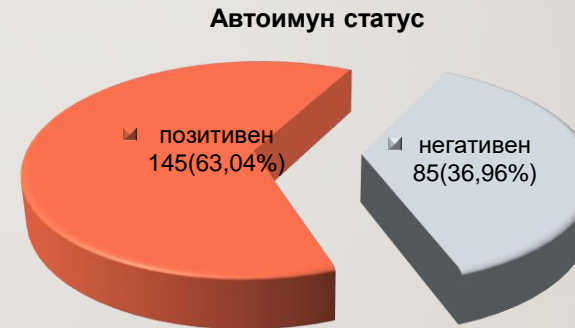
- Anti TPO (35.22%)
- ANA (28%)
- RF (9.57%)

ANA	Група/ group			p-level
	n	ХСУ/ CSU n (%)	КГ/ CG n (%)	
Позитивен/ positive	66	66 (28,7)	0	X ² =45.7 *p=0.000000
негативен / negative	294	164 (71.3)	130 (100)	

RESULTS

AUTOIMMUNE STATUS IN CSU PATIENTS

Автоимун статус/ Autoimmune status	Група/ Group		
	N	ХСУ/ CSU n (%)	КГ/ CG n (%)
позитивен автоимун / positive	145	145 (63.04)	0
негативен автоимун/ negative	85	85 (36.96)	0



RESULTS

AUTOIMMUNE STATUS IN CSU PATIENTS ASSOCIATED WITH AUTOIMMUNE DISEASES

Варијабла/ variable	Автоимун статус/ Autoimmune status		
	N	Позитивен/ positive n(%)	Негативен/ negative n(%)
Лична историја за аутоимуна болест/ Personal history of autoimmune disease			
без присуство/ not present	112	36 (24.83)	76 (89.41)
Присуство/ present	118	109 (75.17)	9 (10.59)
Hashimoto Tireoiditis	66	57 (39.31)	9 (10.59)
Vitiligo	20	20 (13.79)	0
Arthritis Rheumatica	14	14 (9.66)	0
Morbus Crohn	8	8 (5.52)	0
Hashimoto Tireoiditis + Vitiligo	10	10 (6.9)	0
Фамилијарна историја за аутоимуна болест/ Familial history of autoimmune disease			
без присуство/ not present	130	66 (45.52)	64 (75.29)
Присуство/ present	100	79 (54.48)	21 (24.71)
Hashimoto Tireoiditis	72	52 (35.86)	20 (23.53)
Vitiligo	11	10 (6.9)	1 (1.18)
Arthritis Rheumatica	8	8 (5.52)	0
Morbus Crohn	3	3 (2.07)	0
Hashimoto Tireoiditis + Vitiligo	5	5 (3.45)	0
7	1	1 (0.69)	0

- Personal history of autoimmune disease (75.17%)
- Familial history of autoimmune disease (54.48%)

RESULTS

AUTOIMMUNE STATUS IN CSU PATIENTS ASSOCIATED WITH ATOPIC DISEASES

Варијабла/ variable	Автоимун статус/ Autoimmune status			p-level
	N	Позитивен/ positive n(%)	Негативен/ negative n(%)	
Лична историја за атопија/ Personal history of atopy				
Присуство/ present	145	98 (67.59)	47 (55.29)	X ² =3.5 p=0.062
без присуство/ not present	85	47 (32.41)	38 (44.71)	
Фамилијарна историја за атопија/ Familial history of atopy				
Присуство/ present	130	81 (55.86)	49 (57.65)	X ² =0.07 p=0.79
без присуство/ not present	100	64 (44.14)	36 (42.35)	
Лична историја за астма/ Personal history of asthma				
Присуство/ present	127	89 (61.38)	38 (44.71)	X ² =6.02 *p=0.014
без присуство/not present	103	56 (38.62)	47 (55.29)	
Фамилијарна историја за астма/ Familial history of asthma				
Присуство/ present	109	73 (50.34)	36 (42.35)	X ² =1.37 p=0.24
без присуство/ not present	121	72 (49.66)	49 (57.65)	
Лична историја за алергиски ринитис/ Personal history of allergis rhinitis				
Присуство/present	125	83 (57.24)	42 (49.41)	X ² =1.32 p=0.25
без присуство/ not present	105	62 (42.76)	43 (50.59)	
Фамилијарна историја за алергиски ринитис/ Familial history of allergis rhinitis				
Присуство/ present	98	61 (42.07)	37 (43.53)	X ² =0.05 p=0.83
без присуство/ not present	132	84 (57.93)	48 (56.47)	

- Personal history of atopy (67.59%)

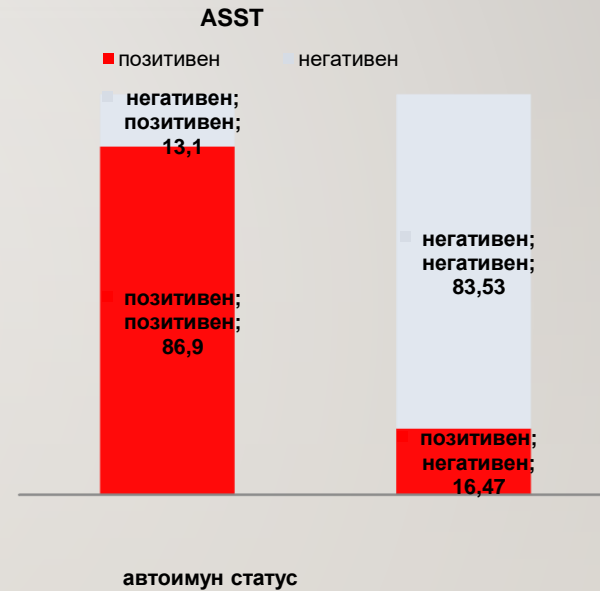
- Personal history of asthma (61.38%)

- Personal history of allergic rhinitis (57.27%)

RESULTS

AUTOIMMUNE STATUS IN CSU PATIENTS AND ASST

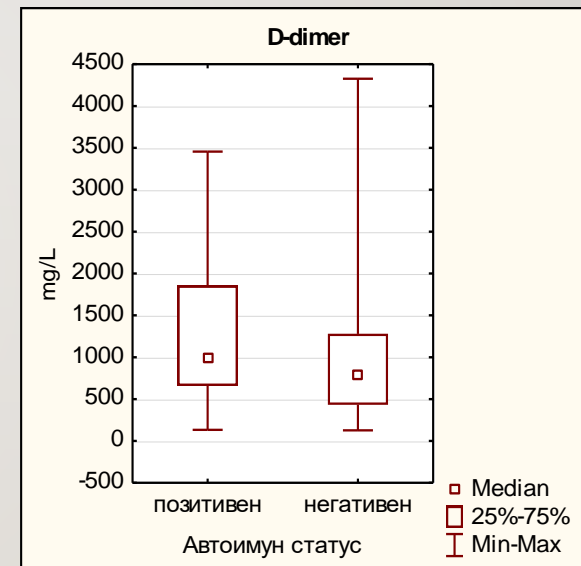
ASST				
Позитивен/ positive	140	126 (86.9)	14 (16.47)	$\chi^2=111.6$ * $p=0.00000$
Негативен/ negative	90	19 (13.1)	71 (83.53)	



RESULTS

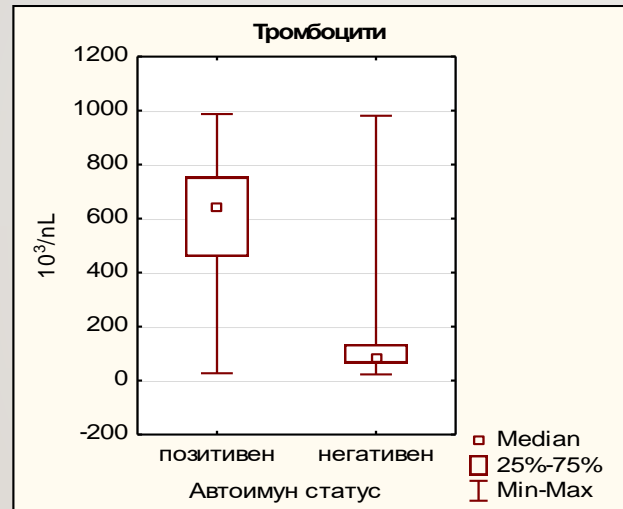
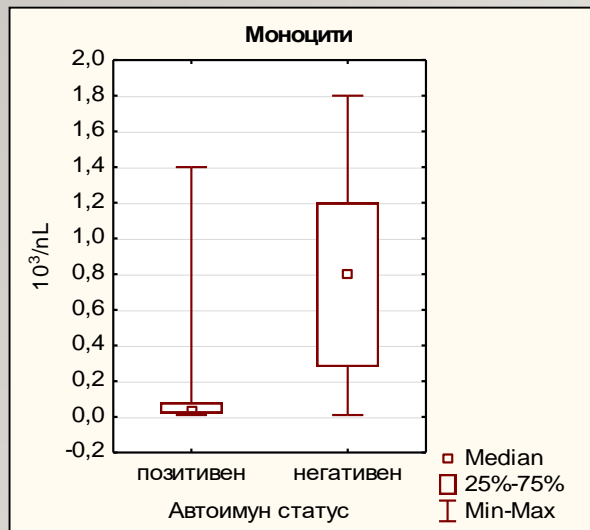
AUTOIMMUNE STATUS IN CSU PATIENTS AND D-DIMER

Варијабла/ variable	Автоимун статус/ Autoimmune status			p-level
	n	Позитивен/ positive	Негативен/ negative	
D-Dimer (mg/L)				
mean ±SD	1280.59 ± 795.0		1025.05 ± 790.5	Z=2.6 *p=0.01
min- max	132 – 3456		126 – 4326	
median (IQR)	997 (657 – 1856)		787 (432 – 1280)	
0 – 500 (%)	n 49	23 (15.86)	26 (30.59)	X ² =6.9 *p=0.0085
>500 (%)	n 181	122 (84.14)	59 (69.41)	



RESULTS

AUTOIMMUNE STATUS IN CSU PATIENTS AND CBC COUNTS



Варијабла/ variable	Автоимун статус/ Autoimmune status		
	n	Позитивен/ positive	Негативен/ negative
Моноцити/ Monocytes ($10^3/nL$)			
mean \pm SD	0.15 \pm 0.3		0.75 \pm 0.5
median (IQR)	0.04 (0.02 – 0.08)		0.8 (0.28 – 1.2)
<0.16 (%)	n	135	121 (83.45)
0.16 – 1 (%)	n	58	18 (12.41)
>1 (%)	n	37	6 (4.14)
Тромбоцити/ Platelets ($10^3/nL$)			
mean \pm SD	587.42 \pm 246.2		156.54 \pm 182.4
median (IQR)	643 (459 – 754)		84 (65 – 134)
<100 (%)	n	69	13 (8.97)
100 – 400 (%)	n	33	12 (8.28)
>400 (%)	n	128	120 (82.76)

RESULTS

AUTOIMMUNE STATUS IN CSU PATIENTS ASSOCIATED WITH CRP, IGE, ANTI-TPO, RF

Варијабла/ variable	Автоимун статус/ Autoimmune status			p-level
	n	Позитивен/ positive	Негативен/ negative	
CRP (mg/l)				
mean ±SD	37.5 ± 27.8		31.5 ± 28.1	Z=1.7
median (IQR)	32 (12 – 65)		23 (7 – 48)	p=0.083
0 – 5 n (%)	40	23 (15.86)	17 (20)	X ² =0.64
>5 n (%)	190	122 (84.14)	68 (80)	p=0.42
IgE(IU/ml)				
mean ±SD	94.3 ± 161.7		485.6 ± 357.4	Z=11.4
median (IQR)	54 (34 – 78)		445 (164 – 786)	*p=0.000000
0 – 100 n (%)	141	128 (88.28)	13 (15.29)	X ² =120.32
>100 n (%)	89	17 (11.72)	72 (84.71)	*p=0.000000
Anti TPO (U/ml)				
mean ±SD	487.6 ± 504.8		100.8 ± 239.2	Z=4.9
median (IQR)	56 (34 – 987)		38 (29 – 52)	*p=0.000001
0 – 60 n (%)	149	74 (51.03)	75 (88.24)	X ² =32.5
>60 n (%)	81	71 (48.97)	10 (11.76)	*p=0.000000
RF (IU/ml)				
mean ±SD	11.7 ± 18.0		4.8 ± 2.9	Z=2.6
median (IQR)	5 (3 – 9)		4 (3 – 7)	*p=0.0098
0 – 15.9 n (%)	208	123 (84.83)	85 (100)	X ² =14.3
>15.9 n (%)	22	22 (15.17)	0	*p=0.00016

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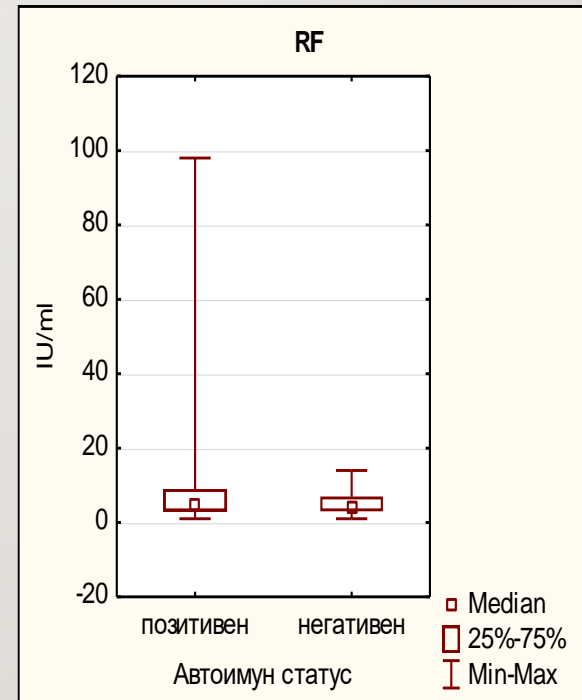
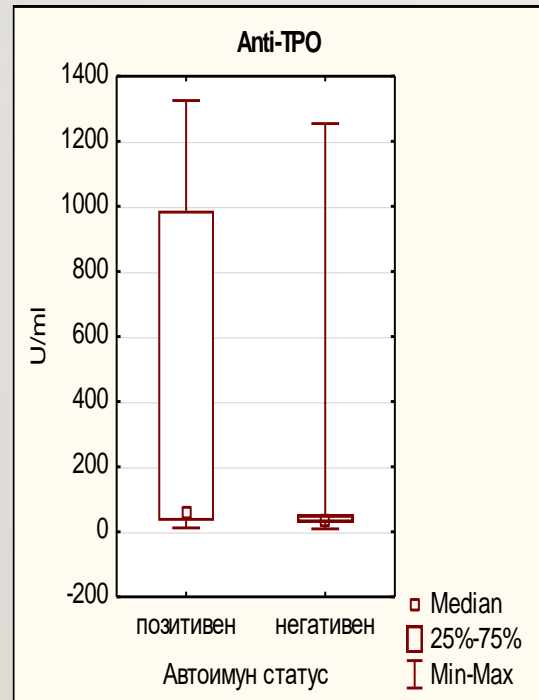
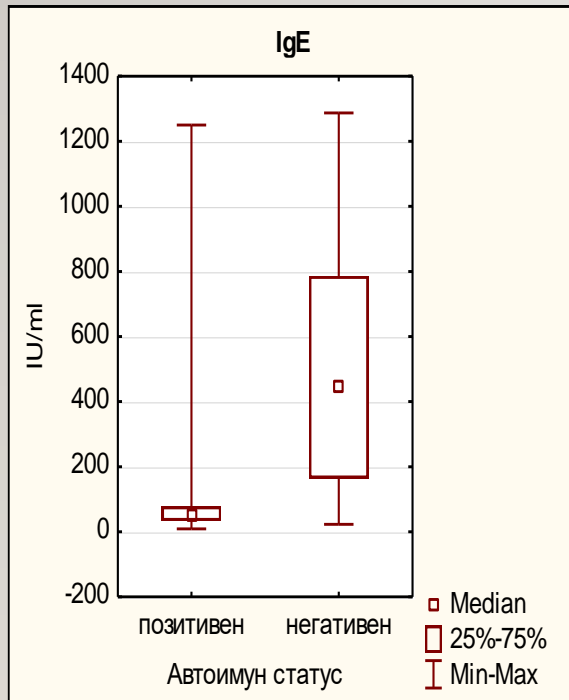
- CRP blood levels (84.14%)
- AntiTPO blood levels (48.97%)
- RF blood levels (15.17%)

Lower:

- IgE blood levels (88.27%)

RESULTS

AUTOIMMUNE STATUS IN CSU PATIENTS ASSOCIATED WITH CRP, IGE, ANTI-TPO, RF



CONCLUSIONS

- We found a relatively high incidence of autoimmune disorders and AAbs (autoimmune status) in patients with CSU.
- In our cohort, we found a correlation between positive ASST and presence of concomitant autoimmune disease and/or AAbs.
- We also found that patients with autoimmune status had higher plasma D-dimer, Platelets, CRP, AAbs levels and lower plasma levels of IgE, Monocytes, than those without autoimmunity.

FUTURE REMARKS

- Since nearly 30 years, several lines of evidence argue for an autoimmune basis of CSU, or at least in a subgroup of them.
- However, the way to distinguish autoimmune and non-autoimmune CSU is still a matter of debate
- The pathogenesis of CSU has not been fully established although it seems clear that different mechanisms are involved.
- This study brings additional evidences over the connection between CSU and autoimmunity.

Fiebigler E, Hammerschmid F, Stingl G, Maurer D. Anti-FcepsilonR1alpha autoantibodies in autoimmune-mediated disorders. Identification of a structure-function relationship. J Clin Invest. 1998 Jan 1;101(1):243-51. doi: 10.1172/JCI5111. PMID: 9421487; PMCID: PMC508561.

THANK YOU FOR YOUR ATTENTION

