

THE ROLE OF ADAMTS13 ACTIVITY IN ASSESSMENT OF SEVERITY IN SHIGA-TOXIN ASSOCIATED AND ATYPICAL HEMOLYTIC UREMIC SYNDROME IN CHILDREN

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INTRODUCTION

- The ADAMTS13 protease limits the growth of blood clots in microcirculation by regulation the functional activity of von Willebrand factor (vWF)
- In hemolytic uremic syndrome (HUS) occlusive thrombus formation occur with participation of the "ADAMTS13 - von Willebrand factor" system, which is of interest

OBJECTIVES

- To establish the role of ADAMTS13 activity in assessing the severity of shiga-toxin associated (STEC-HUS) and atypical HUS (aHUS) in children
- Determine the activity of ADAMTS13 in patients with STEC-HUS and aHUS
- Conduct a comparative analysis of ADAMTS13 activity in patients with STEC-HUS and aHUS
- To establish the dependence of ADAMTS13 activity on the severity of STEC-HUS and aHUS

MATERIALS AND METHODS

- The study included 55 patients with STEC-HUS (mean age 2.8±2,0 years) and 41 with aHUS (mean age 5,2±4,0 years).
- The activity of ADAMTS13 was estimate by FRET (fluorescence resonance energy transfer) using fluorogenic substrate FRET-S-VWF73 (PeptaNova GmbH, Germany), express as percentage (%). The interval of activity of ADAMTS13 in healthy person is 80–122 %.

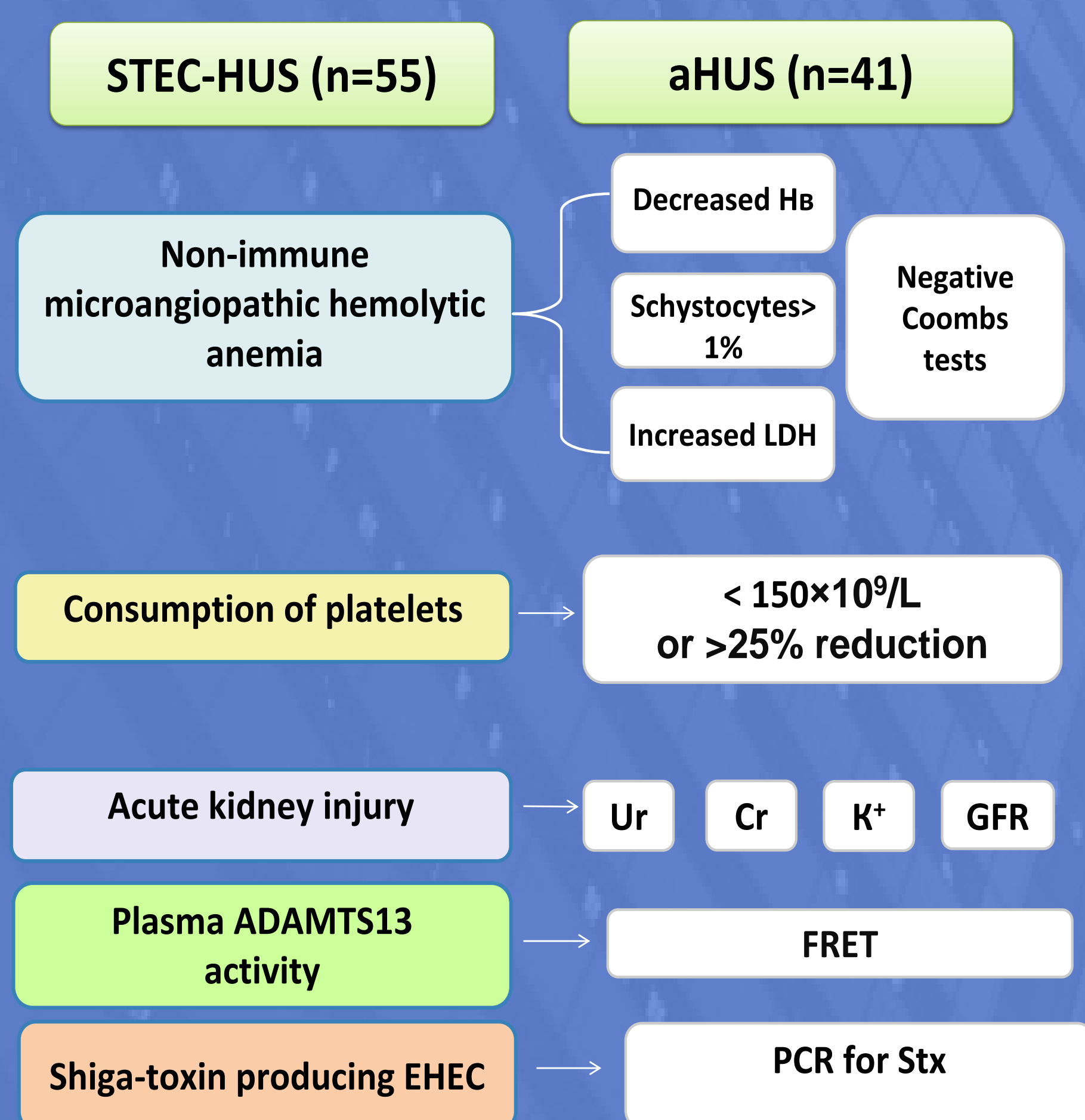
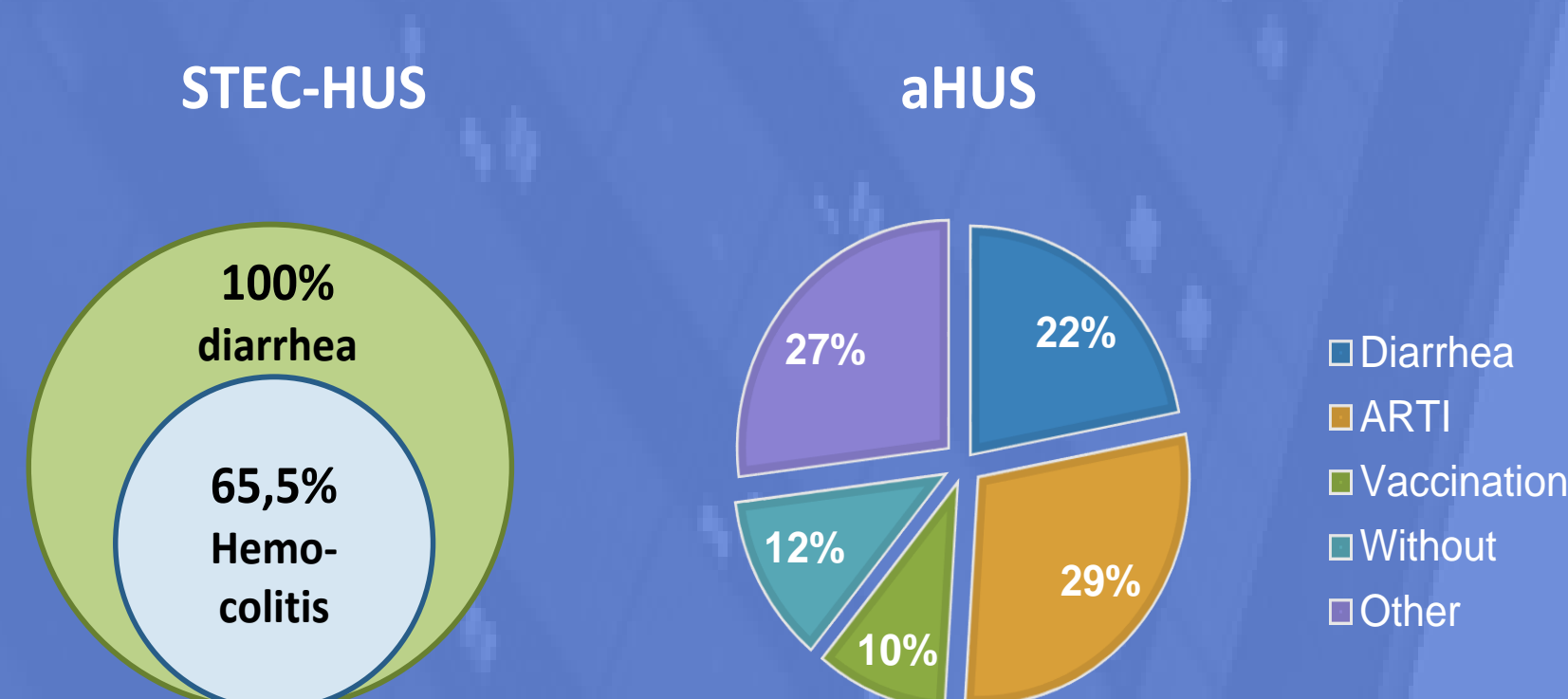


Fig.1 Triggers of the disease



RESULTS

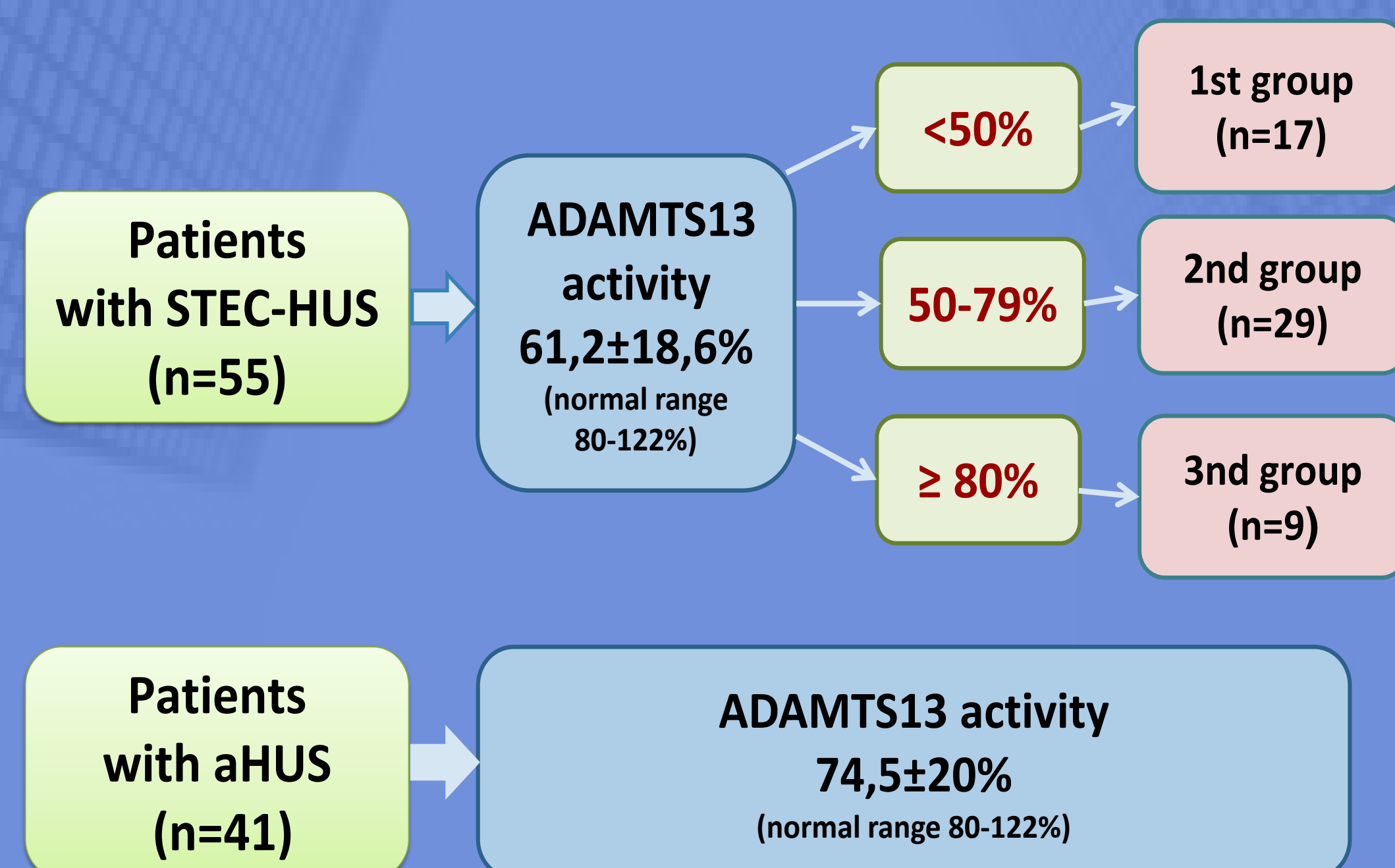
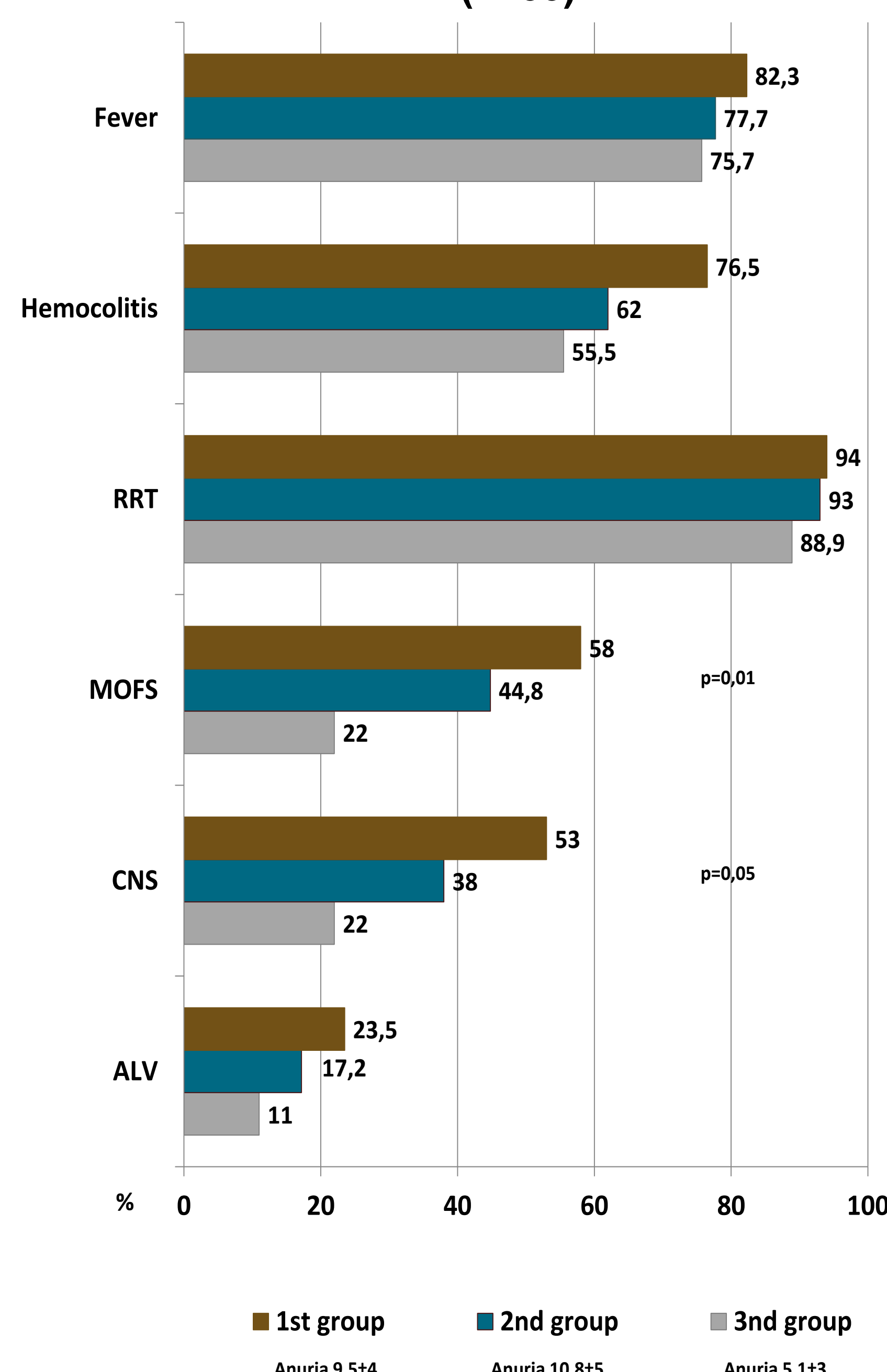


Table 1. Comparison of laboratory characteristics of patients in two groups

Parameters	1 st group (n=17)	2 nd group (n=29)	3 ^d group (n=9)	aHUS (n=41)	p
Hb (g/l)	73±12,2	67,2±15,27	75,4±14,6	62±13	p1,aHUS=0,002 p2,aHUS=0,004
LDH (U/l)	4856,5±1753	2943,2±1300	4076±1850	2580±1831	p1,2=0,0001 p2,aHUS=0,0000 p3,aHUS=0,02 p3,3=0,02
PLT (x10 ⁹ /l)	50,8±24,8	64,14±38,7	68,7±25,6	56±29	
Cr mkmol/l)	412±266	365,8±205	377,5±104	300±211,5	p1,aHUS=0,05
Ur (mmol/l)	30,2±15,5	29,15±13	29,5±7,5	27,3±13	
C3 (mg/dl)	75,2±26,1	78,63±13,7	82,2±12,8	76,6±30	
D-dimer (µg/ml)	4166,3±2801	3162±1808	2855,7±156	2050±1268	p1,aHUS=0,0001 p2,aHUS=0,001 p3,aHUS=0,03
SFMCs (mg%)	10,45±3,1	8,9±4,3	5±1	12±2	p1,2=0,0000 p3,aHUS=0,0000 p2,aHUS=0,0001 p3,3=0,005
Fg (g/l)	3,1±1,2	2,74±0,7	2,2±1	2,7±0,93	p1,3=0,05
ADAMTS13 (%)	39,7±5,3	63±9,2	89,4±5,9	74,5±20,25	p1,aHUS=0,0000 p2,aHUS=0,003 p3,aHUS=0,017

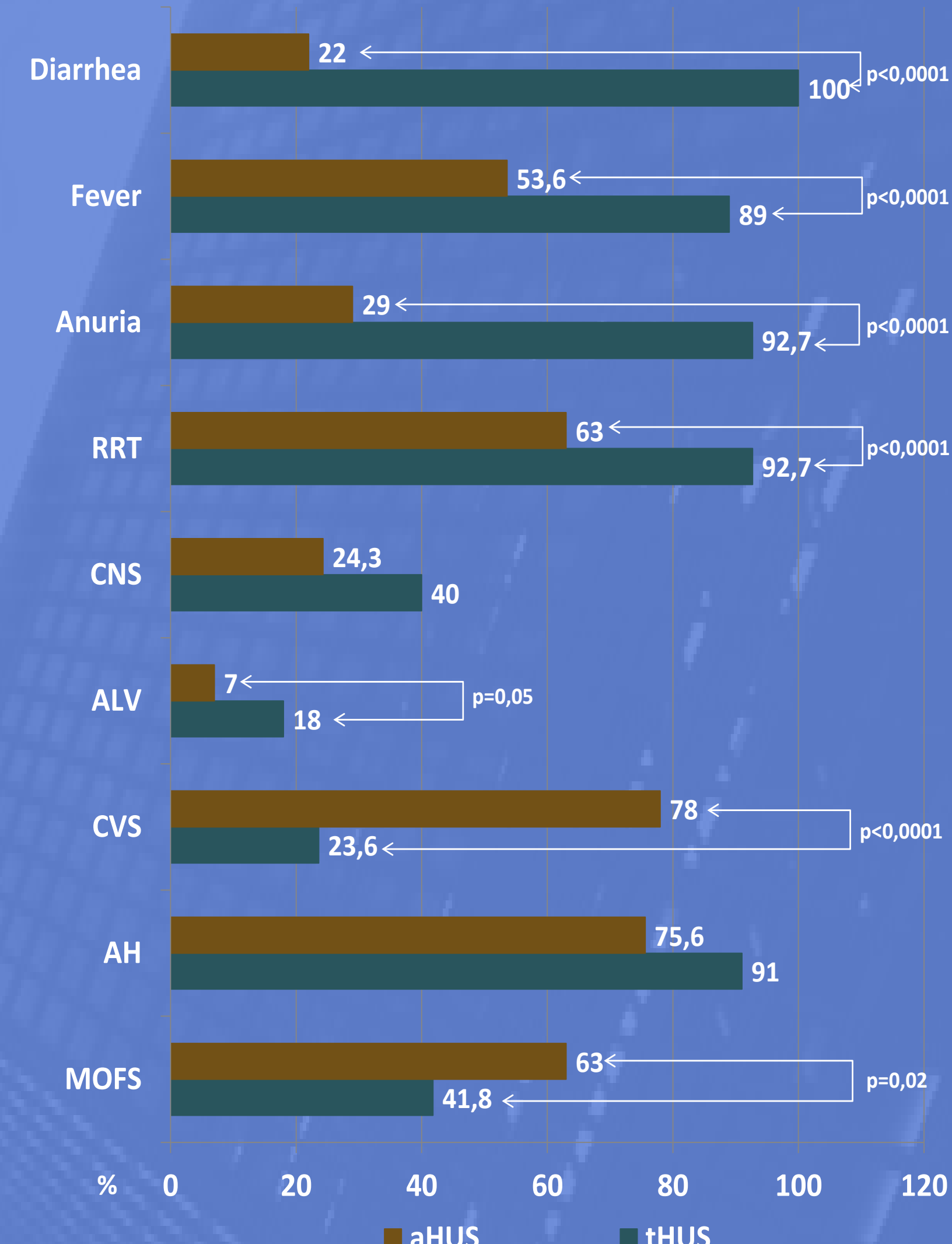
Fg – fibrinogen; SFMCs – Plasma soluble fibrin monomer complexes/fibrinogen;

Fig.2 Clinical characteristics of patients with STEC-HUS depending on ADAMTS13 activity (n=55)



RRT – renal replacement therapy; MOFS – multiply organ failure syndrome; CNS – central nervous system involvement; ALV – artificial lung ventilation

Fig.3 Clinical characteristic of patients with STEC-HUS (n=55) and aHUS (n=41)



RRT – renal replacement therapy; MOFS – multiply organ failure syndrome; CNS – central nervous system involvement; ALV – artificial lung ventilation; AH – arterial hypertension; CVS – cardiovascular system

CONCLUSIONS

- The deficiency of ADAMTS13 activity is detected in 83.6% of patients with STEC-HUS (54,4±13,8) and 66% - with aHUS (63,6±13,5)
- The lowest level of ADAMTS13 activity (39,7±5,3) was reveal in 31% patient with severe acute intestinal infection at the beginning of the desease
- The severity of HUS correlates with ADAMTS13 activity: the STEC-HUS often associated with anuria, CNS symptoms, hypertension, mechanical ventilation and dialysis in compression with aHUS
- In patients with aHUS MOFS and CVS involvement (coronaropathy, dilation of the left ventricule, subendocardial ishemia) presented more often as a type of extrarenal manifestation of the disease. ADAMTS13 activity did not correlate with the severity of the disease
- A more pronounced decrease in ADAMTS13 activity in patients with of STEC-HUS compared with aHUS may be associated with it's consumption due to the expression of super-large multimers vWF under severe endothelial dysfunction, caused by exposure to Shiga toxin
- The deficiency of ADAMTS13 plays a major role in thrombus formation in the microvasculature and thereby organ damage in different forms of HUS

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