

ANALYSIS OF SERUM ACTIVITY OF ADAMTS13 OF SHIGA-TOXIN PRODUCING ESCHERICHIA COLI (STEC) HEMOLYTIC UREMIC SYNDROME (HUS) IN CHILDREN

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INTRODUCTION

- Shiga-toxin associated hemolytic uremic syndrome (STEC-HUS), related to thrombotic microangiopathy, is the most common cause of pediatric acute kidney injury (ARI)
- Shiga toxin produced by Escherichia coli damages the endothelium and activates complement system and platelets, resulting in thrombosis of the microvasculature
- ADAMTS 13 (a disintegrin and metalloprotease, with thrombospondin-1-like domain) - breaks down the multimers of von Willebrand factor (vWF) into smaller units
- ADAMTS13 is a natural regulator of thrombus formation in the microvasculature, it prevents the contact of platelets with endothelium surface
- The activity of ADAMTS13 reduces not only in thrombotic thrombocytopenic purpura, but also in other microangiopathic syndromes such as glomerular disease, sepsis, disseminated intravascular coagulation, cardiovascular and cerebrovascular diseases

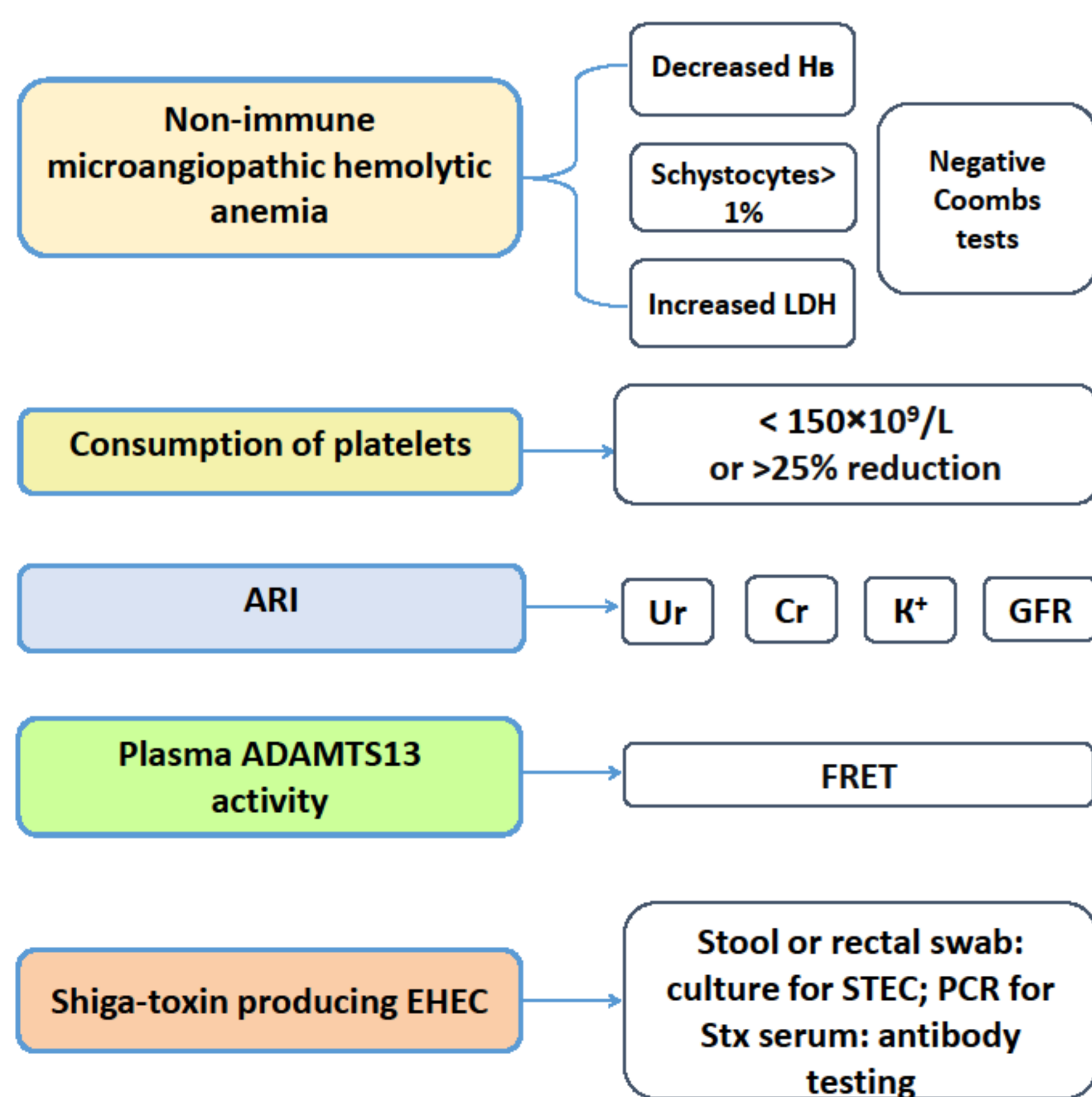
OBJECTIVE

- To determine the extent of reducing the activity of ADAMTS13 in children with STEC-HUS depending on the severity of the disease

MATERIALS AND METHODS

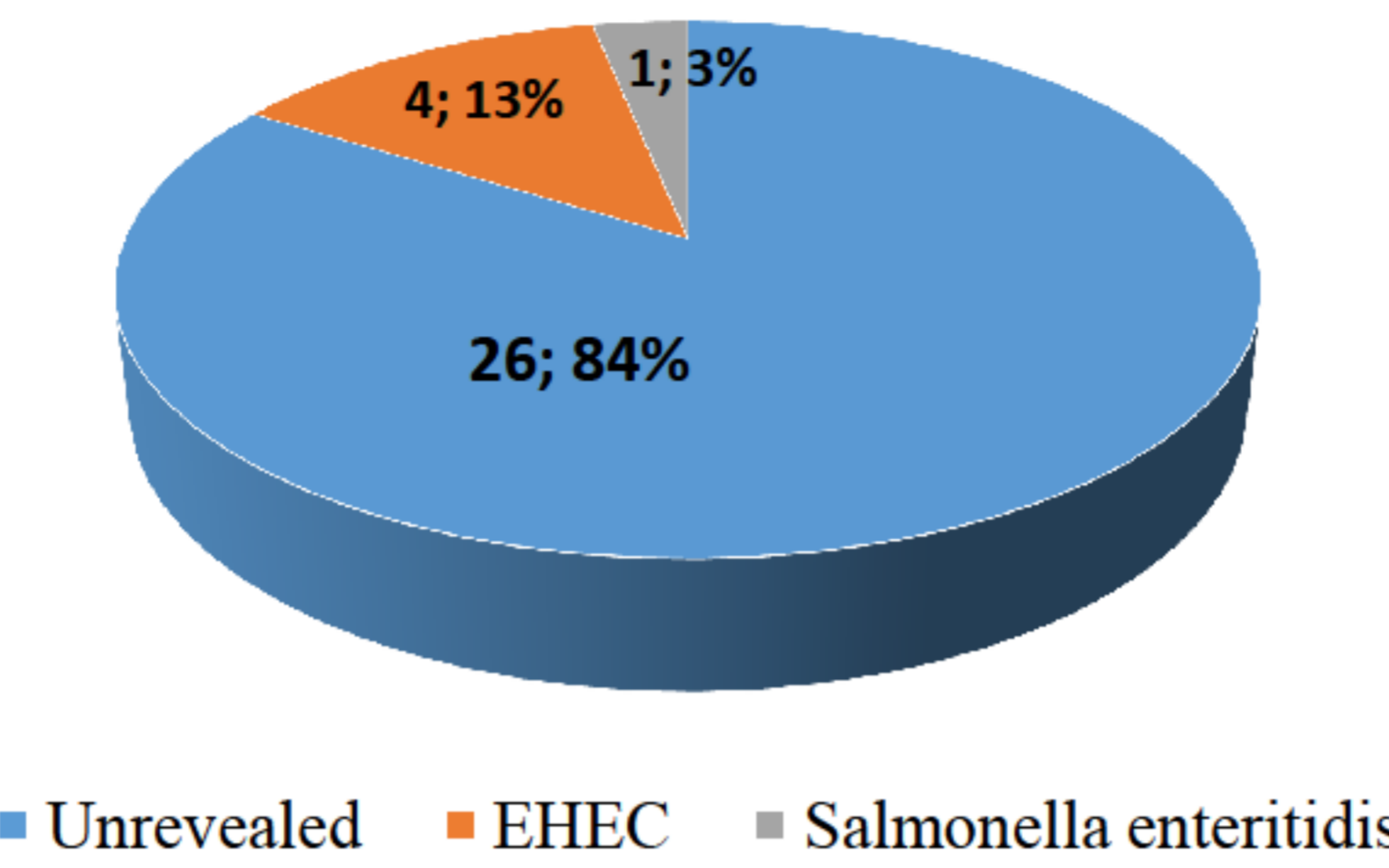
- The study included 31 patients (mean age 2.5±1.7 years) with STEC-HUS: 15 were male (48.3%), 16 – female (51.7%).
- The activity of ADAMTS13 was estimate by FRET (fluorescence resonance energy transfer) using fluorogenic substrate FRET-S-VWF73 (PeptaNova GmbH, Germany), express as percentage (%). The interval of activity of ADAMTS13 in healthy person is 80–122 %.

Patients with HUS (n=31)

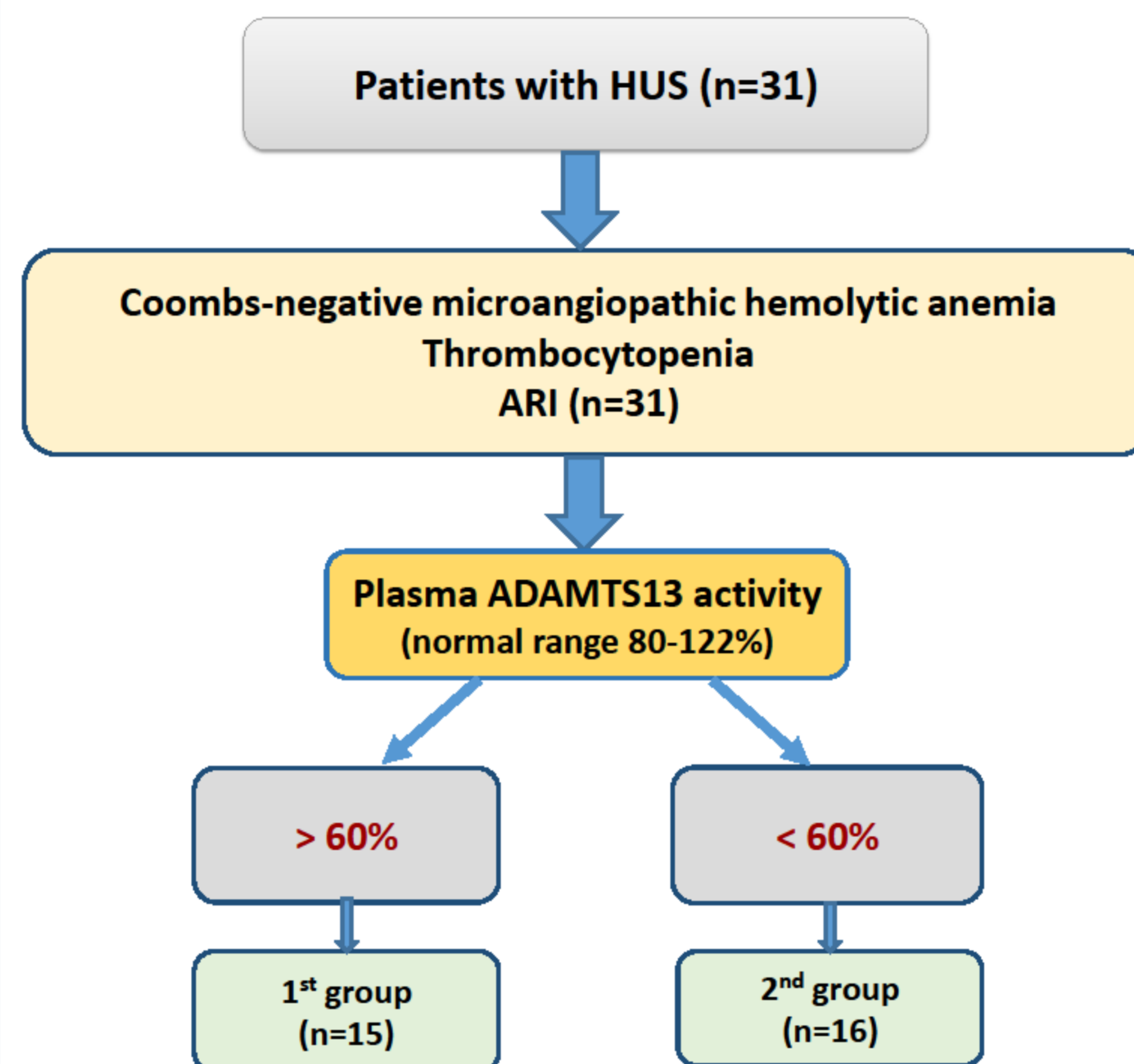


RESULTS

Fig.1 Etiology of acute intestinal infection



- The activity of ADAMTS13 in children with STEC-HUS was 63±18% (35.5-100%). In 15 (48.3%) patients it was higher than 60% but lower than 100% (only in 2 cases corresponded to the norm).



- **1st group:** The development of STEC-HUS in 11 (73.3%) children in this group was associated with mild acute intestinal infections. The duration of anuria was 12.5 ± 14 (3-56) days. CNS involvement (convulsions, coma) was observed in 3 (20%) patients, 4 (26.7%) cases were associated with dysfunction of more than two systems, in 14 (93.3%) children dialysis was conducted.
- **2nd group:** 16 (51.7%) patients presented with severe acute intestinal infections: febrile fever - 100%, gastroenteritis - 12.5%, enterocolitis - 18.8%, hemorrhagic colitis - 68.8%, ileocolonic intussusception - 12.5%. The duration of anuria was 13,5 ± 10.4 (5-22) days, leukocytosis (12.6-46.7 x10⁹/l) and CRP increasing were revealed, and 5 (31.2%) cases complicated by systemic inflammatory response. CNS involvement (seizures, minimally conscious state) developed in 8 (50%) patients, 7 of them required artificial lung ventilation, in 14 (87.5%) cases dialysis was conducted.

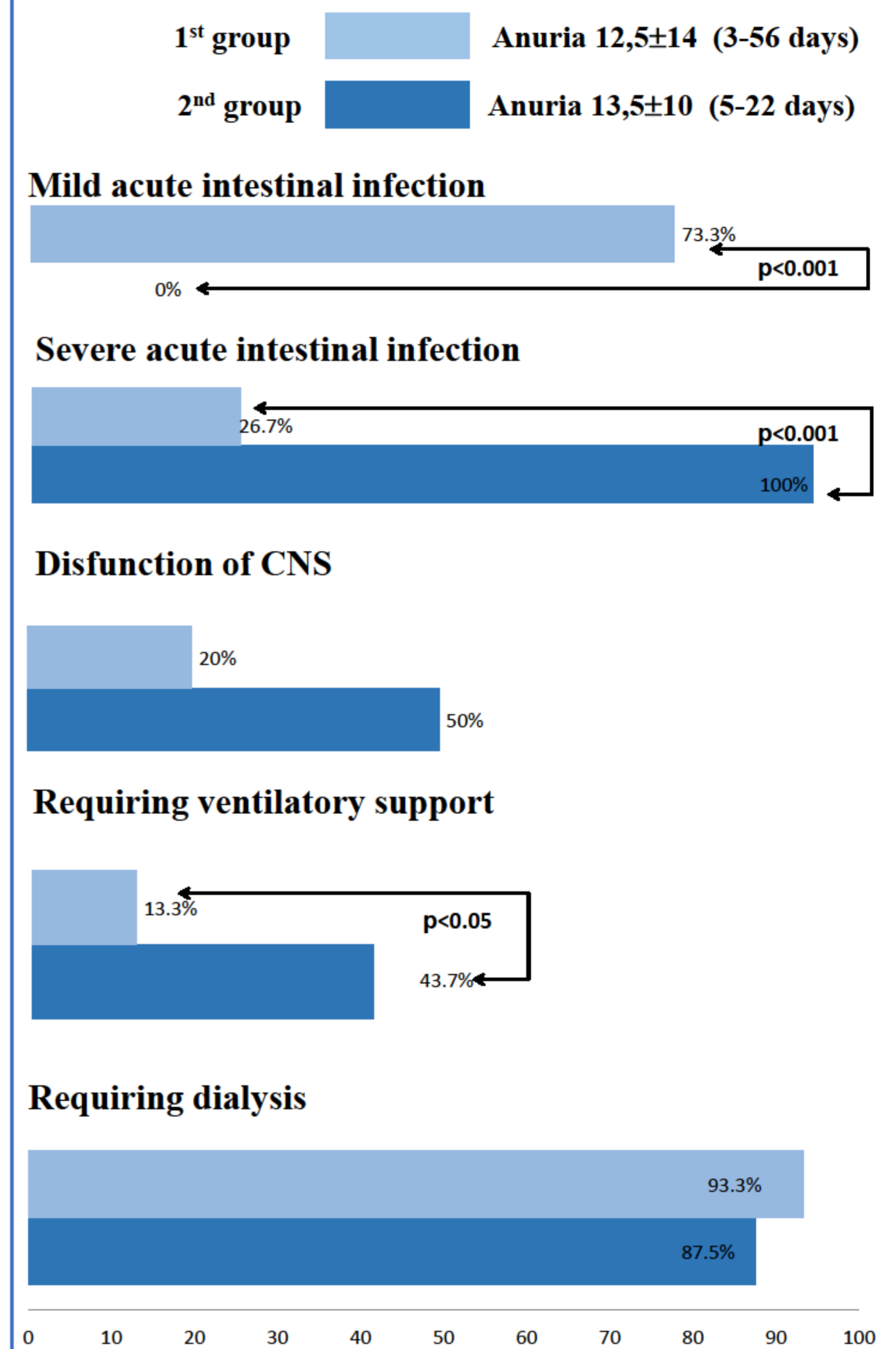
Table 1. Comparison of laboratory characteristics of patients in two groups

Parameter	1 st group (n=15)	2 nd group (n=16)
Hemoglobin (g/l)	79.7±19.2	77.3±19.6
LDH (U/l)	2589.8±795*	3716.7±452.8*
Platelets (x10 ⁹ /л)	58.1±27.6	75.2±40.2
Creatinin (mcmol/l)	378,5±128,8	352.7±174
Urea (mmol/l)	30.8±9.7	29.8±12
D-dimer (ng/ml)	3103.5±2036	3898±2824
SFMCs ¹ (mg%)	10±2.17	7.81±24
ADAMTS13 (%)	77.2±12	47.85±8.3

* - p < 0.05

¹ - Plasma soluble fibrin monomer complexes

Fig.2 Clinical characteristics of patients with HUS (n=30)



CONCLUSIONS

- 90% of patients with typical HUS have a moderate deficiency of ADAMTS13 activity (63±18%)
- Severe acute intestinal infections in 16 patients out of 20 was associated with reducing of ADAMTS13 activity less than 60%
- The severity of HUS is correlated with ADAMTS13 activity: reducing the activity of metalloprotease <60% associated with
 - ✓ 2 times more likely to develop multiple organ dysfunction syndrome
 - ✓ 2.5 – CNS disfunction (seizures, coma)
 - ✓ 5.5 – requiring of ALV
- Excessive consumption of ADAMTS13 in patients with STEC-HUS due to secretion of ultra-large multimers vWF is caused by exposure to infectious triggers in conditions of severe endothelial dysfunction

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