HELLP-SYNDROME A LINK TO AHUS: LABORATORY FEATURES OF PREECLAMPSIA (PE), HELLP-SYNDROME AND PREGNANCY-ASSOCIATED ATYPICAL HEMOLYTIC UREMIC SYNDROME (P-AHUS)

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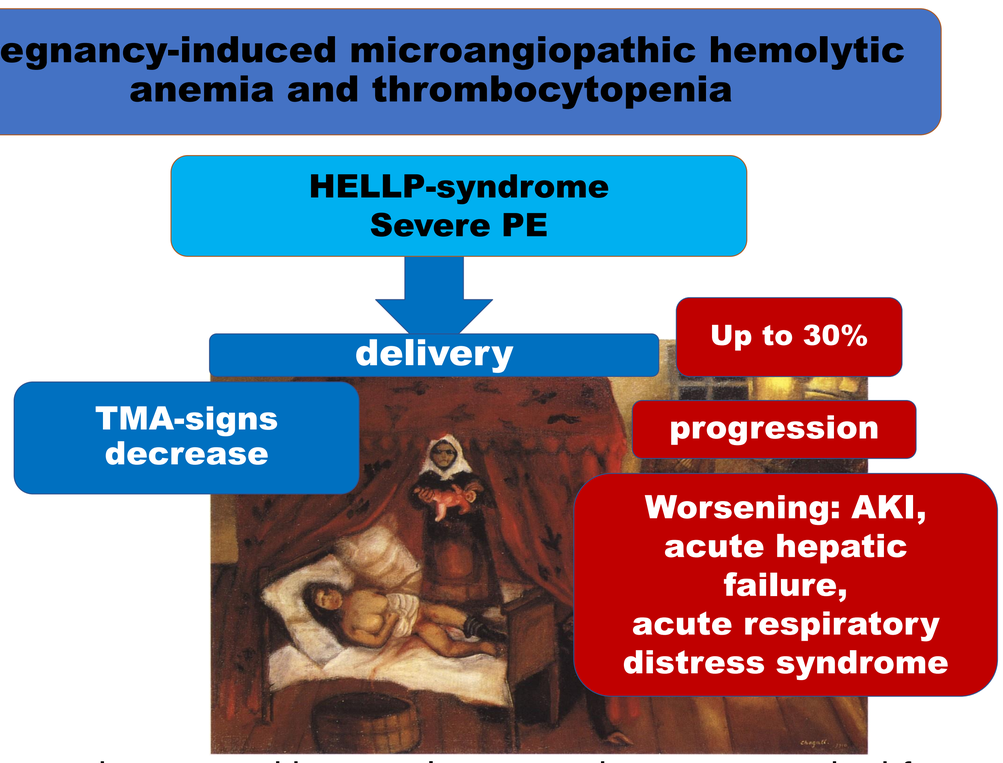
A number of conditions in pregnancy present with microangiopathic hemolytic anemia and thrombocytopenia (MAHAT), including HELLP-syndrome. Recent evidence and clinical similarities suggest a link to P-aHUS, a disease of excessive activation of the alternative complement pathway. HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) is a severe variant of PE that leads to severe morbidity and mortality to both the mother and fetus. Delivery is the treatment of choice of PE and HELLP, but can lead to progression in case of aHUS. Recent studies suggest that HELLP-syndrome may develop without signs of PE and without high sFlt-1-levels. High LDH, liver and kidney dysfunction may be caused by pregnancy-indused MAHAT alone without PE and placenta ischemia.

The aim: to assess and compare the severity of renal and liver manifestation, the blood PLGF and sFlt1 levels in patinets (pts) with HELLP-syndrome, severe PE and aHUS, and evaluate the association markers with the severity of clinical manifestations.



Materials and methods: Women with classic HELLP, P-aHUS, PE with severe features, and women with normal pregnancies were recruited for the retrospective study from September 1, 2013 to December 31, 2016 (treated or consulted in our center via telemedicine). Severe PE diagnosed in accordance with the WHO criteria of 2008. HELLP diagnosed in accordance with Tenessee criteria (laboratory parameters normalized beyond 48-72 hours after delivery without plasma).P-aHUS- rapidly progressive after delivery or onset MAHAT without ADAMTS 13 deficiency.

Results:

Laboratoty features PE,HELLP and P-aHUS patients

	Gr.1 Severe PE (n=20)	Gr.2 HELLP-syndrome (n=36)	Gr.3 P-aHUS (n=31)	Gr.4 Healthy pregnant women (n=28)
mean age, years	29,4 ± 6,0	31,4 ± 5,7	30, 2 ± 8,0	30,8 ± 6,7
Mean gestational age	32± 6,0	31,6± 5,5	35,2± 3,2	37,2± 3,0
Mean nadir platelet count/mm3	192,5 (156-380)	**68,7**(17-96)	**38,5** (4-128)	222,2(210-428)
p1,2; 1,3<0,01, p 2,3 <0,05, p1,4, 2,4, 3,4<0,0005				
Mean nadir Hb, g/L	104,5 (92-144)	**81,2** (55-116)	**56,7** (37-101)	112,5(99-141)
p1,2; 1,3<0,01, p 2,3 <0,05 p2,4, 3,4<0,0005				
LDH, IU/L	396,6 (175-418)	**1349,6**(537-2888)	**2584** (854-11360)	289,2 (115-328)
p1,2; 1,3, 1,4, 2,4, 3,4<0,001, p 2,3 <0,05				
ALT/AST, IU/L	26,2/23,5	**198,1/251,3**	**485,5/518**	22,7/28,4
Peak creatinine, mkmol/l	75,2(52-101)	**131,1**(65-225)	**485**(150-1020)	66,2(48-81)
Mean nadir GFR ml/min (endogenous creatinine clearance)	n=20 88,7 (28-120)	n=16 **51,2** (23-56)	n=6 **12,8** (7-24)	n=20 112,2 (92-240)
PU, g/24h	3,65	2,7	3,7	0,012
Shystocytes,%	0	**0,17**	**1,7**	0
Anti VEGF levels of sFlt-1, sFlt-1/PlGF				
	n=20	n=19	n=2(HELLP onset)	n=28
PlGF	80,55	143,5	186,8	428,2
sFlt-1	14458,70	10608,8	6317,1	62890
sFlt-1/PlGF	439,08	254,4	32,8	7,1
	p1,2; <0,05, p1,4, 2,4<0,0005			

sFlt-1/ PlGF Severe PE 439,08±112,29 > **sFlt-1/ PlGF mild PE 306,62±164,5** > **sFlt-1/ PlGF HELLP 254±93,51**

Gr3 had a poor outcome and most severe course: 26/31 gr.3 -had a PE before delivery (9/31 developed HELLP),10/31 had fetal deaths, 9/31 with signs of severe PE or ACD were urgency delivered, 7/31 had hemorrhage 1000-2000ml. 6/31 had extirpation of uterus. 11/31had signs of heart damage,18/31, a variety of neurological manifestations, 16/31 ARDS, 10/31 renal replacement therapy. However, in addition to PE they had a lot other complement amplifying triggers such as fetal death, placenta abruption, bleeding etc.
Patients gr 2 characterized by less severe course: 5/29 had ACD, 4/29 hemorrhage (1000-2000ml), 5/29 signs of heart damage,16/29, a variety of neurological manifestations, 2/29 ARDS, 2/29 renal replacement therapy, at 2/29 VTE.

Conclusion: P-aHUS and HELLP is life-threatening disorders suggests unique predisposing features and responses to injury. HELLP-syndrome may be one of the stages of atypical HUS and may developed without PE. We suppose the PE and HELLP are various clinical conditions with different outcomes. Based on clinical findings in P-aHUS, we propose a similar mechanism for a pathogenetic role of complement in HELLP.
PE is only trigger or complement-activating condition for development HELLP-syndrome. Depending on the triggering stimuli and vascular bed involved, aHUS or the HELLP syndrome may develop. There were more severe clinical manifestations of renal impairment in all pts with HELLP as compared to women with PE and control gr. The sFlt-1 level was significantly higher in pts with PE as compared with HELLP and HELLP-onset aHUS. The clinical manifestations analysis of PE in both groups indicating more severe its course with HELLP-syndrome that manifests with signs of kidney injury, more frequent complications and adverse perinatal outcomes. Less increased ratio of sFlt-1 / PlGF in gr.1 may confirm that PE is only complement amplifying factor to HELLP-development.

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