

HELLP syndrome, preeclampsia test, gestosis Germany, 3-5 d

General: The HELLP syndrome (hemolysis, elevated liver enzymes and low platelet count) represents a severe, life-threatening pre-eclampsia with typical laboratory parameter constellation; the frequency in all pregnancies is 2-3%. Manifestation is around the 34th week of pregnancy, but can occur post partum as well (24-72 h).

Pathophysiology: the symptom trias of HELLP syndrome results from a disturbed balance between prostacyclin synthesis in the endothelium and thromboxane A2 formation with segmental vasospasms and endothelial lesions. As a consequence of endothelium damages, increased thrombocyte aggregations and fibrin deposits in the terminal vascular system with consecutive microcirculation disturbances are observed. Hemolysis is a result of mechanical and hypoxic damages of RBCs (fragmentocytes). In severe cases a disseminated intravascular coagulation (DIC) is developed.

Clinical signs: main symptoms are usually pains in the right upper abdomen or in the epigastrium, often accompanied by nausea or vomiting, furthermore hypertonia, proteinuria, edema inclination, anemia, hemolysis, general gestosis symptoms, icterus, and hematuria. An unpredictable course as well as the risk of recurrence have to be considered!

Complications: subcapsular hematoma with liver rupture, most severe disseminated intravascular coagulation (DIC).

Differential diagnosis: cholecystitis, cholelithiasis, hiatal hernia, fatty liver, hepatitis, gastritis, pyelonephritis, thrombotic thrombocytopenic purpura, hemolytic-uremic syndrome.

Preeclampsia: Preeclampsia is one of the most life-threatening medical conditions for mother and baby during the later stages of pregnancy. Clinical symptoms starting in the 20th week of pregnancy are mainly hypertonia and proteinuria. Additional complications can be caused by the **HELLP** syndrome, characterized by **H**emolysis, **E**levated **L**iver enzymes and **L**ow **P**latelet count, see above.

In the past years, a significant link was identified between **preeclampsia** and several angiogenic factors such as VEGF (Vascular Epithelial Growth Factor) and PlGF (Placental Growth Factor), its receptor (Flt-1 Fms like tyrosine kinase receptor-1, synonym VEGF receptor-1, Vascular Epithelial Growth Factor Receptor-1) as well as a circulating soluble form of the receptor, s(soluble)Flt-1.

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^ non-accredited parameter

VEGF is an angiogenic factor stimulating vasculogenesis and angiogenesis, creating new blood vessels such as during embryonic development or after injury. PlGF belongs to the VEGF family and is produced by the placental trophoblasts during pregnancy. sFlt-1 is the soluble form of the Flt-1 receptor (soluble Fms-like tyrosine kinase 1, soluble vascular endothelial growth factor (VEGF) receptor 1 (sVEGFR1)), a splice variant of the receptor missing the transmembrane and cytoplasmatic domains.

In patients with both early and late onset preeclampsia significantly elevated levels of Flt and sFlt receptor and lowered levels of PlGF can be detected several weeks before the onset of clinical disease. (Levine RJ et al. Circulating angiogenic factors and the risk of preeclampsia. N Engl J Med 2004; 350:672–683.)

Studies show that the maternal serum levels mirror the placental levels and are significantly altered compared to the levels in women with uncomplicated pregnancies. Based on this and the opposing changes of the two parameters, a **ratio** was calculated to better distinguish between uncomplicated pregnancies and those with preeclampsia. This ratio of sFlt-1/PlGF in maternal serum gives a more reliable prediction of clinical preeclampsia than just measuring the levels of one protein alone. Its value increases 6-8 weeks before the onset of preeclampsia.

■ sFlt1/PLGF ratio in serum

Indication:	Suspicion of preeclampsia, newly appearing elevated blood pressure during pregnancy (systolic >140 mm Hg, diastolic >90 mm Hg), borderline proteinuria without inflammatory infection, gestosis
Preanalytic:	stability: 8h at 2 - 8°C, sample must be frozen for dispatch!
Material:	1 ml serum
Method:	ECLIA
TAT:	Germany, 3 – 5 days
Dimension:	µg/l
Ref.- range:	< 85.0

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^ non-accredited parameter

Levels of sFlt-1 and PLGF in women, who do not develop preeclampsia:

Weeks of pregnancy	soluble Fms-like tyrosine kinase 1-receptor (sFlt-1)	Placental growth factor (PLGF)
10 - 14 weeks	555 - 2361 pg/ml	29.4 - 183 pg/ml
15 - 19 weeks	470 - 2785 pg/ml	65.7 - 203 pg/ml
20 - 23 weeks	649 - 2944 pg/ml	125 - 541 pg/ml
24 - 28 weeks	630 - 3890 pg/ml	130 - 1108 pg/ml
29 - 33 weeks	707 - 6688 pg/ml	73.3 - 1108 pg/ml
34 - 36 weeks	978 - 9921 pg/ml	62.7 - 972 pg/ml
from 37 weeks	1671 - 11324 pg/ml	52.3 - 659 pg/ml

Note: A ratio of 85 or higher indicates the onset of preeclampsia. In cases with suspected preeclampsia but borderline values, the levels should be monitored every 1-2 days. An increase indicates a worsening of the condition.

General laboratory parameters in HELLP syndrome:

Parameter	Levels	Remarks
GOT	increased	
GPT	increased	mostly stronger increase than GOT
LDH	increased	significant increase, relatively non-specific
Hemoglobin	decreased	
Hemoglobin in urine	increased	only in approx. 10% of the cases macrohematuria
Bilirubin (indirect)	increased > 1.2 mg/dl	
Protein in urine	increased	
Peripheral blood smear		fragmentocytes, anisocytosis, poikilocytosis

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Parameter	Levels	Remarks
Haptoglobin	decreased	
Thrombocytes	decreased < 150,000/ μ l	further decreasing within hours, normalizing within 6-11 days post partum
Hematocrit	increased	in progressive course
Uric acid	increased	in progressive course
sFlt-1	increased	
PLGF	decreased	
sFlt-1/PLGF	>85	an increase is observed 6-8 weeks before onset of preeclampsia

^ non-accredited parameter