



## Diagnosis of pregnancy complications (preeclampsia, fetal growth restriction and diabetes) with the sFlt-1/PIGF ratio

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### Objective

To evaluate the diagnostic accuracy of the assay for sFlt-1 and PIGF in singleton pregnancies with hypertensive disorders (PEE), fetal growth restriction (FGR) and diabetes (DM). Reference ranges of the sFlt-1 and PIGF levels in the course of normal pregnancies were generated.

### Methods

The cohort consisted of 912 (100%) pregnant women. Between June 2016 and March 2018 a group of women (308/912, 33.8%, case group) with PEE, FGR and DM was compared to a healthy cohort with uncomplicated pregnancies 604/912 (66.2%, control group). Serum levels of sFlt-1, PIGF and their ratio were analysed with the Kryptor® assay and compared between the two groups.

### Results

The mean age in the case- and control-group was 33.4 years (range 19-46) and 32.5 years (range 20-44), respectively (Mann-Whitney 0.134). Blood samples were collected at 35+6 weeks' (min. 21; max. 42) and 35+5 weeks' gestation (min. 17, max. 41) respectively (Mann-Whitney 0.098). Mean gestational age of delivery in the case-group was 37+6 (min. 24, max. 42) and 39+5 (min. 33, max. 43) in the control-group (Mann-Whitney. 000). Mean birthweight in the case-group was 2817.5g. (min. 220, max. 4780) and 3387.5g. (min. 330, max. 5350 g.) in the control-group (Mann-Whitney. 000). sFlt, sPIGF and sFlt/PIGF ratio among women with pregnancy complications were significantly different (Mann-Whitney. 000) compared to the control-group: mean sPIGF: 149.3 vs. 289.8; sFlt: 6450.5 vs. 3029.7; sFlt/PIGF ratio: 206.2 versus 30.8. In the group of patients with PEE we constructed three groups of values of sFlt/PIGF ratio: those < 156.9; 156.9 – 353.1 and >353.1. The group of patients with sFlt/PIGF ratio lower than 156.9 had negative proteinuria in 95.4% of cases and were at low risk for developing PEE (no disorder in 98.2%). The group of patients with a ratio between 156.9 – 353.1 had positive proteinuria in 28.6% of cases and risk of developing PEE was 3.6% till 34 weeks' gestation and 29.1% after 34 weeks' gestation. Comparison of the sFlt/PIGF ratio between PEE-related outcomes including FGR or PEE and healthy controls showed a high diagnostic accuracy with an area under the curve (AUC) of 0.814 for PEE and 0.748 for FGR. For DM the AUC was 0.485. The average time from presentation to hospital to delivery was significantly lower in complicated pregnancies.

### Conclusion

Our study of 912 patients generated ranges and clinical cut-offs for sFlt, sPIGF and sFlt/PIGF ratio in control- and case groups. We found differences in the absolute values when comparing to earlier published ranges of sFlt, sPIGF and sFlt/PIGF ratio. For the Kryptor system, a cut-off value of 156.9 seems to have high clinical specificity and negative predictive value in the diagnosis of preeclampsia.