Background
There is no tool to accurately predict who is at risk of developing neurologic complications of preeclampsia, and there is no objective method to determine disease severity.

Objective
We assessed whether plasma concentrations of the cerebral biomarkers neurofilament light, tau, and glial fibrillary acidic protein could reflect disease severity in several phenotypes of preeclampsia. Furthermore, we compared the cerebral biomarkers with the angiogenic biomarkers soluble fms-like tyrosine kinase 1, placental growth factor, and soluble endoglin.

Study Design
In this observational study, we included women from the South African Preeclampsia Obstetric Adverse Events biobank. Plasma samples taken at diagnosis (preeclampsia cases) or admission for delivery (normotensive controls) were analyzed for concentrations of neurofilament light, tau, glial fibrillary acidic protein, placental growth factor, soluble fms-like tyrosine kinase 1, and soluble endoglin. The cerebrospinal fluid concentrations of inflammatory markers and albumin were analyzed in a subgroup of 15 women. Analyses were adjusted for gestational age, time from seizures and delivery to sampling, maternal age, and parity.

Results
Compared with 28 women with normotensive pregnancies, 146 women with preeclampsia demonstrated 2.18-fold higher plasma concentrations of neurofilament light (95% confidence interval, 1.64–2.88), 2.17-fold higher tau (95% confidence interval, 1.49–3.16), and 2.77-fold higher glial fibrillary acidic protein (95% confidence interval, 2.06–3.72). Overall, 72 women with neurologic complications (eclampsia, cortical blindness, and stroke) demonstrated increased plasma concentrations of tau (2.99-fold higher; 95% confidence interval, 1.92–4.65) and glial fibrillary acidic protein (3.22-fold higher; 95% confidence interval, 2.06–5.02) compared with women with preeclampsia without pulmonary edema; hemolysis, elevated liver enzymes, and low platelet count; or neurologic complications (n=31). Moreover, angiogenic markers were higher, but to a lesser extent. Women with hemolysis, elevated liver enzymes, and low platelet count (n=20) demonstrated increased plasma concentrations of neurofilament light (1.64-fold higher; 95% confidence interval, 1.06–2.55), tau (4.44-fold higher; 95% confidence interval, 1.85–10.66), and glial fibrillary acidic protein (1.82-fold higher; 95% confidence interval, 1.32–2.50) compared with women with preeclampsia without pulmonary edema; hemolysis, elevated liver enzymes, and low platelet count; or neurologic complications. There was no difference shown in the angiogenic biomarkers. There was no difference between 23 women with preeclampsia complicated by pulmonary edema and women with preeclampsia without pulmonary edema; hemolysis, elevated liver enzymes, and low platelet count; or neurologic complications for any of the biomarkers. Plasma concentrations of tau and glial fibrillary acidic protein were increased in women with several neurologic complications compared with women with eclampsia only (Figure).

Conclusion
Plasma neurofilament light, glial fibrillary acidic, and tau were candidate biomarkers for the diagnosis and possibly prediction of cerebral complications of preeclampsia.
**FIGURE**

Differences between women with different phenotypes of preeclampsia

The *scatterplots* show the plasma concentrations with medians for NfL (A), tau (B), and GFAP (C). The outliers were removed from the figure but included in the statistical analyses: preeclampsia (n = 31; preeclampsia without pulmonary edema, HELLP syndrome, or neurological complications), pulmonary edema (n = 23), HELLP syndrome (n = 20), and neurologic complications (n = 72).

GFAP, glial fibrillary acidic protein; HELLP, hemolysis, elevated liver enzymes, and low platelet count; NfL, neurofilament light; ns, nonsignificant.


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