

Contribution of Placental Mitochondrial Damage to Preeclampsia

Fetal

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INTRODUCTION

- •Preeclampsia (PE) is a hypertensive disorder of pregnancy with accompanying proteinuria and/or systemic disturbances; and the leading cause of maternal and perinatal mortality worldwide. ¹
- •The underlying etiology of preeclampsia is poorly understood. Prior research indicates that the underlying mechanism is related to placentally derived oxidative stress. ^{2,3}
- •Recent cardiovascular studies have implicated mitochondrial dysfunction and reactive oxygen species (ROS) as a key players in the pathogenesis of hypertension and cardiac disease. Preeclampsia may follow a similar mode of pathogenesis. ^{4,5}

HYPOTHESIS

Pregnancies complicated by PE have decreased mitochondrial integrity as manifested by increased mitochondrial DNA (mtDNA) damage, and increased fission which results in decreased ATP production.

METHODS

Maternal and Fetal Placenta tissues:
Preeclampsia/Non-Preeclampsia

Mitochondrial DNA
integrity:

Mitochondrial DNA
Damage (PCR
based assay)

A. Fusion

OPA1

Mitochondrial
fission/fusion:

Mitochondrial
fission/fusion:

• Mitofusin-1 and

Dynamin Related

Protein (DRP) 1

immunoassays

Quantitative PCR Assessment of Mitochondrial DNA Damage: Control Pre-eclampsia 1.0 40 90.5 p=0.011 Pre-eclampsia 1.0 p=0.049

Figure 1. Preeclamptic samples have increased mitochondrial DNA damage. In aggregate, the control group (N=6) has 0.032 lesions per 10Kb, and the preeclamptic group (N=6), 0.236 lesions/10Kb (~7-fold increase, p=0.011). When divided into fetal and maternal groups (control and preeclamptic groups N=3 for maternal and fetal), fetal placenta shows significantly greater lesions (p=0.049) while maternal placenta does not display statistically significant differences in DNA lesions.

Maternal

Maternal + Fetal

Relative expression of Mitofusin (MFN) and Phosphorylated Dynamin Related Protein-1

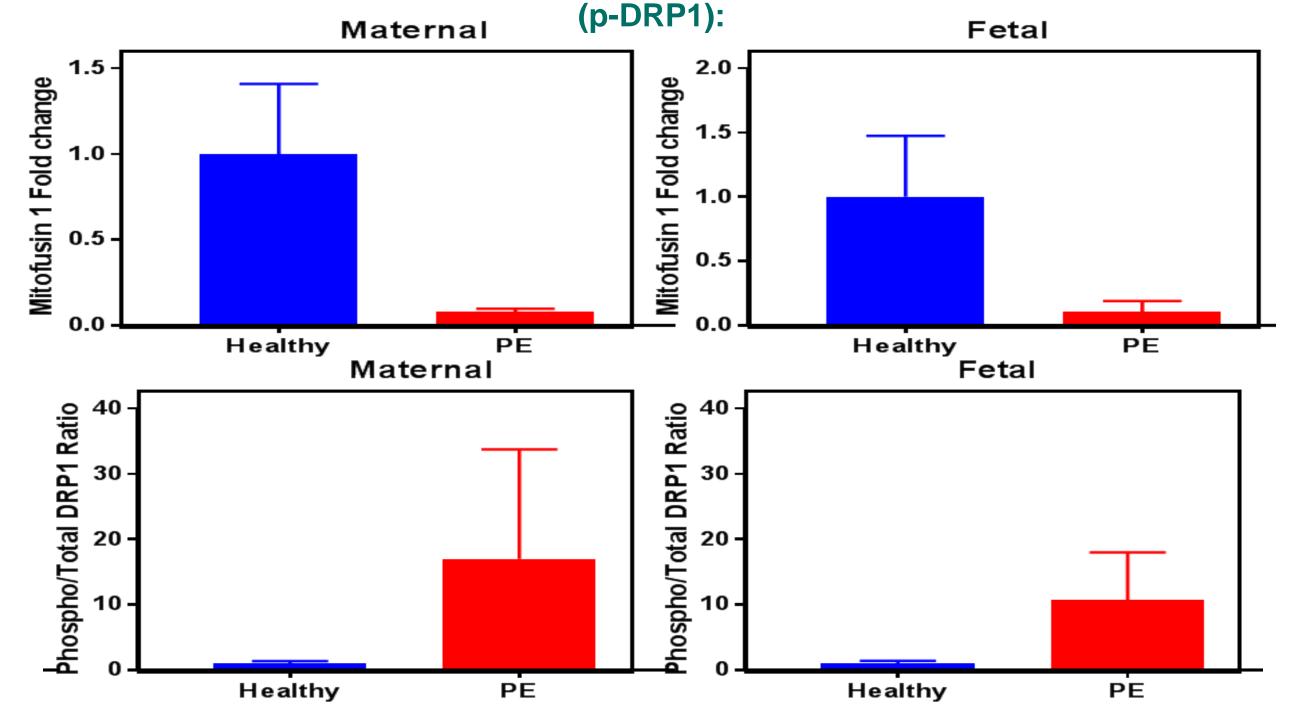
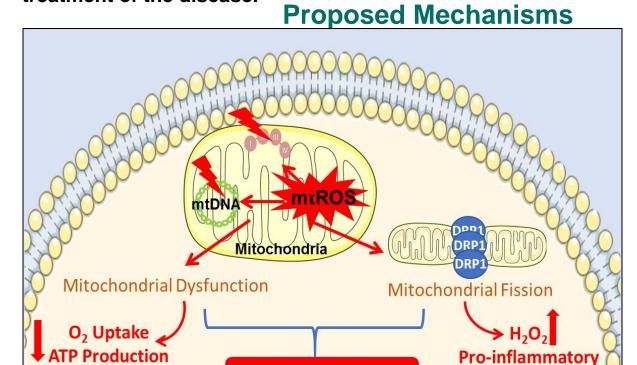


Figure 2. Preeclamptic samples have an increase in mitochondrial fission relative to controls. Preeclamptic samples displayed lower levels of MFN expression (N=18, p=0.08), and significantly greater levels of pDRP. (N=18, p=.05). This overall trend was maintained in both fetal and maternal groups.

CONCLUSION

- •In patients with preeclampsia, greater levels of mitochondrial DNA damage are observed than in placenta from healthy pregnancies.
- •Preeclamptic mitochondria express greater levels of phosphorylated DRP and less MFN than healthy controls. This indicates greater levels of mitochondrial fission, an indicator of mitochondrial stress.
- •Mitochondrial dysfunction may play a key role in the pathogenesis of PE and may serve as a novel target for the treatment of the disease.



 Accumulation of reactive oxygen species in placental mitochondria leads to damage of mtDNA, and respiratory chain.

PREECLAMPSIA

- As result, mitochondrial fission increases and respiratory function declines.
- ROS and pro-inflammatory mediators produced during these processes ultimately contribute to the systemic inflammatory response that is seen during preeclampsia.

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