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Title: Mechanism of Thrombin Generation in Morbidly Obese Pregnant Women

Introduction: A significant number of maternal mortality due to venous thromboembolism involved obese women. There is limited information regarding thromboprophylaxis in this setting. Non-obstetric data suggests that natural anticoagulants free tissue factor pathway inhibitor (TFPI) and free protein S, together with coagulant factor VII are all important determinants of thrombin generation.

Aim: This study investigated the mechanisms involved in thrombin generation within morbidly obese pregnant women.

Method: We recruited thirty normal weight (n=30) and thirty morbidly obese (n=30) pregnant women. With informed consent, venous blood (4.5mls) was taken using 3.13% sodium citrate as anticoagulant. Samples were centrifuged at 4°C for 20 minutes at 2000g. The resulting platelet poor plasma were stored at -80 °C until assay. Factor VII, free protein S, free TFPI and thrombin generation were measured in plasma from obese and normal weight pregnant women using commercially available ELISA assays.

Results: There is a significant reduction in Free Protein S and Free TFPI levels in the obese compared to the normal weight group of pregnant women, $85.60 \pm 21.39\%$ vs $112.69 \pm 10.58\%$ ($P < 0.0005$) and $10.24 \pm 2.38 \text{ ng/ml}$ vs $13.15 \pm 4.22 \text{ ng/ml}$ ($P < 0.002$), respectively. We also observe significant increase of Factor VII $186.57 \pm 56.20\%$ vs $119.71 \pm 37.87\%$ ($p < 0.005$) and endogenous thrombin potential $3228.33 \pm 373.31 \text{ nM.min}$ vs $2896.50 \pm 389.46 \text{ nM.min}$ ($p < 0.05$) in the obese compared to the normal weight group of pregnant women.

Conclusion: Reduced natural anticoagulants and increased coagulant Factor VII all contribute to increased thrombin generation in the morbidly obese pregnant women. This will further inform thromboprophylaxis measures in the obese parturient.