**Oestrogen-Responsive miR-365a-3p and miR-548aa Expression is Increased in Whole Blood From Females on Hormone Based Contraceptives and During Pregnancy**

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**Aim:**High oestrogen levels are associated with increased risk of venous thromboembolism (VTE), however, precise mechanisms remain unclear. microRNAs (miRs) are implicated in disease progression and are detectable in blood, thus may be potential biomarkers for monitoring oestrogen-mediated VTE. This study determined the expression of three selected oestrogen-responsive miRs (miR-365a-3p, miR-548aa and miR-494-3p), and their respective coagulation factor targets, in cohorts with low or high oestrogen levels.

**Method:**Whole bloods in PAXgene RNA, citrate and EDTA plasma from healthy women without contraceptives (controls) (n=31), on hormone-based contraceptives (n=17), and during pregnancy and post-partum (n=15). Expression of miR-365a-3p, miR-548aa, and miR-494-3p was measured using RT-qPCR. A coagulation factor panel was assessed by ELISA, STA-R® analyser, and Ceveron® alpha thrombin generation assay. One-way ANOVA was used for statistical analysis.

**Results:**Compared to healthy controls, women on contraceptives and during pregnancy had increased expression of miR-365a-3p and miR-548aa (2-fold). Conversely, miR-494-3p expression remained unchanged. Tissue factor and factor VIII activity were increased by ~3.5-fold (P<0.05, contraceptive group) and ~2-fold (P<0.05, the third trimester), respectively, in those with high oestrogen levels. In contrast, total and free protein S decreased by ~30-80 % (P<0.01) in the same group. Moreover, total thrombin generation was ~1.4-fold higher in cohorts with high oestrogen levels (P<0.005), compared to controls.

**Conclusion:**

Females with high oestrogen levels had increased miR-365a-3p and miR-548aa expression, but not miR-494-3p. In *in vitro* models, oestrogen-mediated miR expression is different, suggesting oestrogen response may be tissue specific. Furthermore, increased tissue factor and factor VIII activity as well as decreased protein S may contribute toward the hypercoagulable state in those with high oestrogen levels. Taken together, this pilot data suggests oestrogen-responsive miR-365a-3p and miR-548aa may be potential biomarkers to identify the hypercoagulability in cohorts with high oestrogen levels, and warrants further investigation.