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Spencer, R. orcid.org/0000-0002-3019-0322 and Farrelly, R. Maternal plasma extracellular vesicle size and concentration in pregnancies affected by early-onset fetal growth restriction. In: BMFMS Annual Conference 2022, 17 Nov 2022 - 18 Nov 2023, Birmingham, UK. (Unpublished)

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Proceedings Paper:

Farrelly, R. and Spencer, R. orcid.org/0000-0002-3019-0322 (2023) Maternal plasma extracellular vesicle size and concentration in pregnancies affected by early-onset fetal growth restriction. In: BJOG: An International Journal of Obstetrics and Gynaecology. BMFMS Annual Conference 2022, 17-18 Nov 2022, Birmingham, UK. Abstracts of the 2022 BMFMS meeting, 130 (S1). Wiley , pp. 91-92.

<https://doi.org/10.1111/1471-0528.17419>

This is a conference poster originally presented at the BMFMS Annual Conference 2022, 17-18 Nov 2022, Birmingham, UK.

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Maternal plasma extracellular vesicle (EV) size and concentration in pregnancies affected by early-onset Fetal Growth Restriction (FGR)

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Study Aims

- 1) Characterise the size and concentration of maternal plasma EVs in pregnancies affected by early onset FGR
- 2) Compare EV profiles using indicators of more severe disease and by fetal sex

Method

Maternal plasma samples collected in 18 pregnancies diagnosed with early-onset fetal growth restriction (estimated fetal weight <3rd centile at 20+0-26+6 weeks)

EVs were isolated using IZON size exclusion columns, pooled into fractions 7-12 and concentrated.

EV samples were measured for mean and mode size within the sample as well as concentration (particles per ml) using Nanoparticle Tracking Analysis.

Results

- Gestation at delivery ranged from 25+0-38+6 weeks with seven male and eleven female infants.
- EV size and concentration did not differ by fetal sex or between pregnancies with or without hypertensive disease (Figure 1), raised umbilical artery pulsatility index or placental classification of maternal vascular malperfusion.
- EV size and concentration showed no association with birthweight z score (BWz) overall, but in the eight pregnancies unaffected by hypertensive disease there was a significant positive association between modal EV size and BWz ($p=0.072$) (Figure 2).
- This association remained significant after adjustment for gestational age

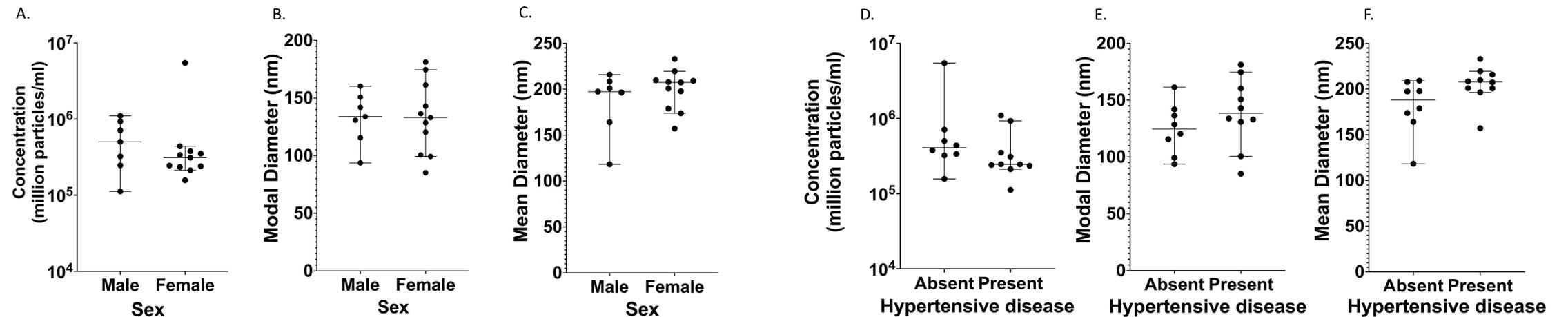


Figure 1. Maternal plasma EV concentration, modal diameter, and mean diameter in FGR (n=18) by sex and by the absence and presence of hypertensive disease. Concentration (million particles/ml) is plotted on a log(10) axis, with horizontal lines denoting median and error bars denoting 95% confidence interval. There is no significant difference between the properties of EVs; A. concentration ($p=0.2854$), B. modal diameter ($p>0.9999$) and C. mean diameter ($p=0.3749$) in maternal plasma of male (n=7) and female (n=11) FGR pregnancies. Nor is there a significant difference between the properties of EVs; D. concentration ($p=0.1457$), E. modal diameter ($p=0.2370$) and F. mean diameter ($p=0.0545$) in maternal plasma EVs in FGR pregnancies with (n=10) or without (n=8) hypertensive disease during pregnancy.

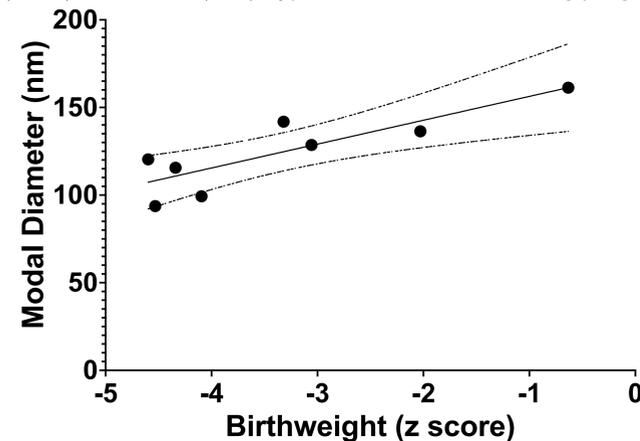


Figure 2. Linear regression of maternal plasma EVs in FGR samples with the absence of hypertensive disease in pregnancy (n=8) against Marsal chart birthweight z score values. Concentration (million particles/ml) is plotted on a log(10). Linear regression analysis is represented by the solid line, with dashed lines representing 95% confidence interval. Strong positive association between birthweight z score and modal diameter of EVs in this cohort ($p=0.0072$, Confidence interval: 5.274 to 21.96)

Conclusion

Maternal EV size and concentration do not appear to be affected by many indicators of FGR severity. In non-hypertensive pregnancies, modal diameter increased with increasing birthweight z score.