**IMPACT OF PERITONEAL FLUID CERAMIDES ON ENDOMETRIOSIS ASSOCIATED INFERTILITY (EAI)**

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**Introduction:**
Endometriosis is associated with marked subfertility, altered oocyte quality and accumulated levels of potentially oocytotoxic compounds in peritoneal fluids (PF). Due to the juxtapositioning of ovaries and released oocytes to the PF, an altered PF may have detrimental effects on the maturation potential of oocytes thereby impairing fertilization. Ceramides have been found to be toxic to oocytes and embryos both in vivo and in vitro. Little is known, however, how PF ceramides contribute to oocyte quality and plausibly EAI. We hypothesize that a defective peritoneal environment rift with increased very-long-chain ceramides influences subfertility in endometriosis, and that these ceramides may alter oocyte maturation potential.

**Materials/Patients and Methods:**
A case-control study of 39 women undergoing laparoscopic procedures for various indications were recruited into the study in the KK Women’s and Children’s Hospital, Singapore. Women between 22-40 years were recruited, presence of endometriosis recorded and staged, and fertility characteristics collected. Subjects were excluded if FSH > 10 IU/L or had male infertility contributions. PF were aspirated during laparoscopy and had their lipids profiled via liquid chromatography-mass spectrometry. Linear regression was conducted to identify PF ceramides associated with EAI.

To assess the effect of ceramides on oocyte maturation potential, more than 900 denuded GV oocytes from BALB/c mice were matured in PF of subjects and also in the presence of ceramides at increasing concentrations for 14 hours. Assessment of GV to MII oocyte maturation potential was made via polar body extrusion.

**Results:**
Comparing infertile women with endometriosis and non-endometriotic women, three very-long chain ceramides, C22:0 ceramide (p=0.006), C24:0 ceramide (p=0.006) and C24:1 ceramide (p=0.026) were significantly associated with a combined Area Under Curve (95% CI) of 0.95 (0.83-1.00). With non-endometriosis subjects as reference, Odds Ratios indicated that C24:1 ceramide increases risk (OR=1.017, 95% CI: 1.00-1.033), whereas Cer C22:0 ceramide (OR=0.927, 95% CI: 0.86-0.995) and C24:0 ceramide (OR=0.989, 95% CI: 0.976-1.001) mitigate the risk.

PF from women with and without endometriosis compromised the maturation potential of murine oocytes. The maturation potential of murine oocytes varied with exposure to the very long chained ceramides. By 14 hours, C24:1 ceramide arrested oocytes mainly at GV and MI stage, obtunding maturation to MII. Conversely, C24:0 ceramide significantly improved the maturation potential of GVs to MIIIs in a dose-dependent manner relative to vehicle control.

**Conclusion:**
Collectively, the results suggest that any underlying pathology in the peritoneal fluids of women with endometriosis may contribute to compromised oocyte maturation potential and potentially affect fertility in various stages of reproduction, whether by natural conception or IVF, in the ampulla contiguous to the peritoneal cavity where fertilisation typically takes place.

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**Keywords :**
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References :

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