## Serum MicroRNA and Inflammatory Mediators: Diagnostic Biomarkers for Endometritis in Arabian Mares

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Abstract: The identification and quantification of serum microRNA (miRNA) from mares with endometritis might serve as useful and implementable clinical biomarkers for the early diagnosis of endometiritis. Aims of the current study were (I) to study the expression pattern of eca-miR-155, eca-miR-223, eca-miR-17, eca-miR-200a, and eca-miR-205, and (II) to determine the levels of interleukin 6 (IL-6), prostaglandins (PGF $_2\alpha$  and PGE $_2$ ), in the serum of Arabian mares with healthy and abnormal uterine status (endometritis). This study was conducted on 80 Arabian mares (4-14 years old). Mares were divided into 48 subfertile mares suspected of endometritis and 32 fertile at stud farms. The criteria for mares to be enrolled in the endometritis group were that they had been bred three or more times unsuccessfully in the breeding season or had a history of more than one year of reproductive failure. In addition, two or more of the following criteria on a checklist were present: abnormal clinical findings, transrectal ultrasonographic uterine examination showed abnormal fluid in the uterus (echogenic or ≥2 cm in diameter), positive endometrial cytology; and bacterial and/or fungal growth. Serum samples were collected for measuring IL-6, PGF<sub>2</sub>α, and PGE<sub>2</sub> concentrations, as well as serum miRNA isolation and quantitative real-time PCR. Serum concentrations of IL-6, PGE<sub>2</sub>, and PGF<sub>2</sub> $\alpha$  were higher (P  $\leq$  0.001) in mares with endometritis compared to the control healthy ones. The expression profile of eca-miR-155, eca-miR-223, eca-miR-17, eca-miR-200a, and eca-miR-205 increased (P≤0.001) in mares with endometritis compared to the control ones. To the best of our knowledge, this is the first study that revealed that serum miRNA and serum inflammatory mediators (IL-6, PGE<sub>2</sub>, and PGF<sub>2</sub>α) could be used as non-invasive gold standard biomarkers, and therefore might be served as an important additional diagnostic tool for endometritis in Arabian mares. Moreover, estimation of the serum concentrations of serum miRNA, IL-6, PGE2, and PGF2α is a promising recommended tool during the breeding soundness examination in mares.

Keywords: Arabian Mares, endometritis, inflammatory mediators, serum miRNA

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