Oral microbiome alterations in adolescents and young adults with endometriosis

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Introduction/Background
While immune dysregulation is postulated to contribute to endometriosis and other chronic inflammatory diseases have been linked with oral flora dysbiosis, the association between endometriosis oral microbiome and endometriosis is unclear. Thus, the objective of this study was to identify endometriosis-associated oral microbiota that could lead to a non-invasive diagnostic.

Materials and Methods
We performed whole genome sequencing(target:40 million reads/sample) on salivary DNA from 89 laparoscopically-confirmed endometriosis (>90% rASRM stage I/II) patients and 101 frequency-matched controls who participated in the WERF EPHect compliant Women's Health Study: From Adolescence to Adulthood. To determine the oral microbiome profiles associated with endometriosis, we used general linear models and examined the differences in oral microbiome diversity and composition between endometriosis patients and controls. False discovery rate(FDR) was used for multiple testing correction.

Results
Median age was 21 years (IQR=17-27 years) for endometriosis cases and 23 years (IQR=20-27 years) for controls. Endometriosis case-control status was significantly associated with the beta diversity or the overall oral microbial composition (p=0.006) accounting for 1.3% of variation between groups. Among individual species, *Veillonella parvula* (β=1.16, FDR=0.04) was more abundant in endometriosis cases compared to controls, while *Alloprevotella* (β=-2.00, FDR=0.049), was less abundant in endometriosis cases compared to controls. *Prevotella loescheii* (β=0.99, FDR=0.07) and *Prevotella oulorum* (β=0.81, FDR=0.14) were suggestively more prevalent in endometriosis cases compared to controls, while *Prevotella intermedia*(β=-1.26,FDR=0.04), *Eubacterium sulci* (β=-1.46,FDR=0.049), *Prevotellaceae* (β=-1.22, FDR=0.10), and *Catonella massiliensis* (β=-1.27, FDR=0.10) were less prevalent. Among endometriosis cases, *Provetella salivae* abundance was associated with having life-impacting pain(β=1.25, FDR=0.11).

Conclusion
We identified multiple endometriosis-associated oral microbes which have been linked with autoimmune disorders/systemic inflammation, providing biological insight into systemic immune dysregulation in endometriosis. With validation in larger independent cohorts, our results could lead to novel non-invasive biomarkers for earlier diagnosis of endometriosis that could be applied to a younger population.

Key words
Endometriosis, oral microbiome, non-invasive biomarker