**HYPOTHESIS:**
Periodontal bacteria can enhance cancer cells invasiveness.

**BACKGROUND/AIMS:**
Oral squamous cell carcinomas (OSCCs) are the most common cancers that affect the oral epithelium. Periodontitis is a chronic infection that affects the periodontium. The association between periodontal disease/bacteria and oral cancer have been reported in many studies. However, the effect of interaction between periodontal bacteria and cancer cells on oral cancer progression and aggressiveness is not well studied. Therefore, we aim to investigate the effect of four major periodontal bacteria on cancer cell pathology.

**METHODS:**
Three oral cancer cell lines OQ01, BHY and HN were used. Periodontal bacteria *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia*, and *Fusobacterium nucleatum* were used to infect the oral cancer cell lines as polybacterial infection. Further analysis was done on OQ01 with mono bacterial infection. The level of different cytokines (TNF, IL-6, IL8 and TGF-β) were quantified in the culture supernatants after 6 and 24 h using ELISA. The relative change in expression of seven different oncogenes (MMP1, MMP9, MYC, JAK1, ZEB1, STAT3 and CD70) was measured using RT-PCR in cell lysate after RNA isolation.

**RESULTS & Conclusion**
OQ01 alone showed significantly enhance IL-8 secretion (P= 0.0003); however, enhanced TFG-β secretion was detected in all cell lines tested. Polybacterial infection of oral cancer cell lines with these pathogens also upregulated MMP1 and MMP9, which are known to enhance cancer cell invasiveness. In addition, the expression of ZEB1, an oncogene known to induce epithelial mesenchymal transition in cancer cells, and MYC, JAK1 and STAT3, oncogenes involved in cell survival, were all significantly enhanced in polybacterial infected cancer cells. Moreover, periodontal bacteria appeared to induce CD70/CD27 pathway, a pathway that is known to help cancer cells escape immune surveillance.

Further analysis using OQ01 cells in mono bacterial infection showed that *F. nucleatum* alone had the same or greater effect as polybacterial infection with all 4 bacteria. These results showed that *F. nucleatum* was the main periodontal bacteria responsible for inducing invasive phenotype in these oral cancer cells. This study demonstrated that the interaction between oral cancer cells and periodontal bacteria might be both cancer cell and bacteria-specific. Our study can be highly useful in examining how modulating oral cancer environment can improve treatment outcome.