To evaluate the possible role of high risk Human Papilloma viruses (HPV) 16 and 18 in oral squamous cell carcinomas (OSCC), 40 SCCs and 15 benign lesions were analyzed for the presence of HPV DNA. The investigation followed a case-control design. Cases consisted of patients diagnosed with OSCCs. Controls were patients diagnosed with benign oral lesions. Information concerning all study subjects were retrieved from hospital records. Genomic DNA was isolated from the formalin-fixed paraffin embedded tissue (FFPET) specimens and tested for detection of HPV DNA by polymerase chain reaction (PCR). Pearson Chi-square test for statistical significance (P value), with the 95% confidence level and confidence intervals were used. HPVDNA was detected in 15% of cases (six out of 40 cases), and none of controls (n=15), P <0.0001. Among the six positive cases four were HPV type 18 and the remaining two were type 16. These results provide evidence supporting causal association between HPV infection and oral SCC in Sudan.