

## INTISARI

**Latar Belakang:** Karsinoma sel skuamosa penis (KSSP), meskipun jarang, menimbulkan beban morbiditas dan dampak terhadap kualitas hidup yang bermakna. Bukti terdapat perbedaan molekuler dan luaran klinis antara KSSP terkait dan tidak terkait HPV dimana teridentifikasi jalur sinyal yang berbeda pada kedua subentitas patogenesis tersebut. Namun, hasil penelitian terdahulu inkonsisten, sehingga masih belum dapat dipahami. Secara global, sekitar 40–50% KSSP berhubungan dengan HPV, namun data di Indonesia, khususnya Yogyakarta, data masih terbatas. Karakteristik klinikopatologis KSSP berdasarkan status HPV dan distribusi genotipe HPV wilayah lokal penting untuk memberikan pemahaman epidemiologi, serta memperkuat strategi diagnostik, tatalaksana, dan pencegahan.

**Tujuan:** Penelitian ini bertujuan untuk menyelidiki perbedaan karakteristik klinikopatologis antara KSSP terkait dan tidak terkait HPV serta mendeskripsikan distribusi genotipe HPV pada kasus KSSP di Yogyakarta.

**Metode:** Studi potong lintang dilakukan pada 31 kasus KSSP di Laboratorium Patologi Anatomi, RSUP Dr. Sardjito periode 2017-2024. Deteksi dan identifikasi 28 genotipe HPV dilakukan dengan *real-time* PCR. Kasus diklasifikasikan terkait HPV jika mengandung hrHPV, sedangkan temuan lrHPV saja atau negatif dikategorikan sebagai tidak terkait HPV. Analisis perbedaan karakteristik klinikopatologis dilakukan dengan uji *T-independent*, *Fisher's exact* (nilai  $p < 0,05$ ), dan perhitungan *odds ratio*. Distribusi genotipe dilaporkan deskriptif.

**Hasil:** Dari 31 kasus, mayoritas kasus KSSP di Yogyakarta adalah tidak terkait HPV (54,8%). Terdapat perbedaan bermakna terkait ukuran tumor  $>4$  cm ( $p = 0,0497$ , OR = 6,07) dan stadium klinis III-IV ( $p = 0,0069$ , OR = 25) cenderung terjadi pada kelompok tidak terkait HPV, sedangkan variabel lain berupa usia, lokasi, subtipe dan derajat histopatologi, invasi lokal (ke pembuluh darah/limfe/saraf), maupun keterlibatan tumor pada limfonodi tidak menunjukkan perbedaan bermakna. Distribusi genotipe HPV didominasi oleh HPV-11 (33,3%), diikuti oleh HPV-6 (22,2%), HPV-18 (19%), HPV-31 (6,3%), HPV-16 (3,2%), HPV-33, HPV-35, HPV-45, HPV-58, HPV-59, HPV-44, HPV-61, HPV-66, dan HPV-68 (masing-masing 1,6%), dengan HPV-18 sebagai tipe hrHPV tersering.

**Kesimpulan:** KSSP tidak terkait HPV lebih dominan di Yogyakarta dengan karakteristik klinikopatologis yang cenderung lebih agresif, ditandai dengan ukuran tumor yang lebih besar dan stadium yang lebih lanjut. Distribusi genotipe HPV menunjukkan pola unik dengan dominasi tipe lrHPV (HPV-11 dan HPV-6), serta HPV-18 (hrHPV tersering) yang berbeda dari pola global. Temuan ini memberikan wawasan penting mengenai epidemiologi molekuler KSSP di Yogyakarta dan dapat berkontribusi terhadap pengembangan strategi tepat sasaran untuk populasi Yogyakarta. Studi multisenter masih diperlukan.

## ABSTRACT

**Background:** Penile squamous cell carcinoma (PSCC), although rare, imposes a significant morbidity burden with substantial impact on quality of life. Evidence reveals molecular and clinical outcome differences between HPV-related and HPV-independent PSCC, which identify distinct signaling pathways in these two pathogenesis sub-entities. However, previous research findings remain inconsistent, thus limiting our understanding. Globally, approximately 40–50% of PSCC cases are associated with HPV infection, yet data from Indonesia, particularly Yogyakarta, remain limited. Characterizing clinicopathological features based on HPV status and local HPV genotype distribution is crucial for providing epidemiological insights and strengthening diagnostic, therapeutic, and preventive strategies.

**Objective:** This study aimed to identify differences in clinicopathological characteristics between HPV-related and HPV-independent PSCC and to describe HPV genotype distribution in PSCC cases in Yogyakarta.

**Method:** A cross-sectional study was conducted on 31 PSCC cases at the Anatomical Pathology Laboratory, Dr. Sardjito Hospital during 2017-2024. Detection and identification of 28 HPV genotypes were performed using real-time PCR. Cases were classified as HPV-related if containing hrHPV, while those with only lrHPV or negative results were categorized as HPV-independent. Analysis of clinicopathological differences was performed using independent t-test, Fisher's exact test ( $p$ -value  $<0.05$ ), and odds ratio calculation. Genotype distribution was reported descriptively.

**Result:** Of 31 cases, the majority of PSCC in Yogyakarta were HPV-independent (54.8%). Significant differences were observed in tumor size  $>4$  cm ( $p = 0.0497$ , OR = 6,07) and clinical stage III-IV ( $p = 0.0069$ , OR = 25), which were more frequent in the HPV-independent group, while other variables including age, location, histopathological subtype and grade, local invasion (vascular/lymphatic/neural), and lymph node involvement showed no significant differences. HPV genotype distribution was dominated by HPV-11 (33,3%), HPV-6 (22,2%), HPV-18 (19%), HPV-31 (6,3%), HPV-16 (3,2%), HPV-33, HPV-35, HPV-45, HPV-58, HPV-59, HPV-44, HPV-61, HPV-66, and HPV-68 (each 1,6%), with HPV-18 being the most common hrHPV type.

**Conclusion:** HPV-independent PSCC predominated in Yogyakarta with more aggressive clinicopathological characteristics, marked by larger tumor size and advanced stage. HPV genotype distribution showed a unique pattern with dominance of lrHPV types (HPV-11 and HPV-6) and HPV-18 as the most common hrHPV, differing from global patterns. These findings provide important insights into the molecular epidemiology of PSCC in Yogyakarta and may contribute to targeted strategy development for the Yogyakarta population. Multicenter studies are still needed.