Prevalence and Genotype Distribution of HPV in Cytology Specimens Containing Atypical Glandular Cells: A Case Control Study

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Introduction

- HR-HPV responsible for ≥99% of all cervical cancer, with HPV 16/18 causing ~70%

- Pap test: Marked decline in the incidence of squamous cell cervical cancers, **but** incidence of glandular cell cancers has increased[1, 2]

- Atypical glandular cell (AGC) grade Pap test results are rare (0.2-0.7%) but 38% represent a corresponding high-grade lesion on biopsy[3, 4]

- AGC management guidelines: Colposcopy, endocervical sampling & HR-HPV DNA testing[5]

Objective

- Determine prevalence & genotype distribution of HPV in AGC-grade cytology specimens compared to women whose Pap smears were negative for intraepithial lesion or malignancy (NILM), with ages known for both groups of women.

Methods

- Collected residual, de-identified AGC & NILM cytology specimens
- DNA was extracted using QIAamp MinElute Media Kit and analyzed by PCR using Linear Array HPV Genotyping and Detection Test Kits
- Multivariate logistic regression compared HPV prevalence and genotype distribution between cases and controls to generate age-adjusted odds ratios (ORadj) and 95% confidence intervals (CI)

Results

Table 1. Study Sample Description

	Total number tested	Mean age (yr)	Median age (yr)	Age range (yr)
AGC-grade cases	53	57	56	18-95
NILM-grade controls	338	45	43	20-91

Table 2 A. Percent of specimens containing detectable levels of HR-HPV DNA

HR-HPV Status *	AGC-grade cases	NILM-grade controls
	%	%
Positive	34	7.4
Negative	66	92.6
Total	100	100

*Regardless of LR- HPV co-infection

Distribution of HR-HPV types

Table 2 B. Percent of specimens containing detectable levels of LR-HPV DNA

| LR HPV Status *	AGC-grade cases	NILM-grade controls
	%	%
Positive	13.2	17.2
Negative	86.8	82.8
Total	100	100

*Regardless of HR-HPV co-infection

Distribution of LR-HPV types

Table 3. Multivariate age-adjusted logistic regression analysis comparing risk of finding HR-HPV or LR-HPV DNA in AGC-grade cases compared to NILM-grade controls

HPV Type(s)	*ORadj (95% CI)	P value
Any HR HPV (inc. 16/18)	9.11 (4.08, 20.33)	< 0.001
HR HPV 16/18 only$^\phi$	40.10 (10.73, 149.88)	< 0.001
Any LR HPV	0.91 (0.35, 2.31)	0.834

* ORadj; adjusted Odds Ratio, 95% CI; 95% Confidence Interval,
ϕ; Irrespective of other HR HPV or LR HPV types
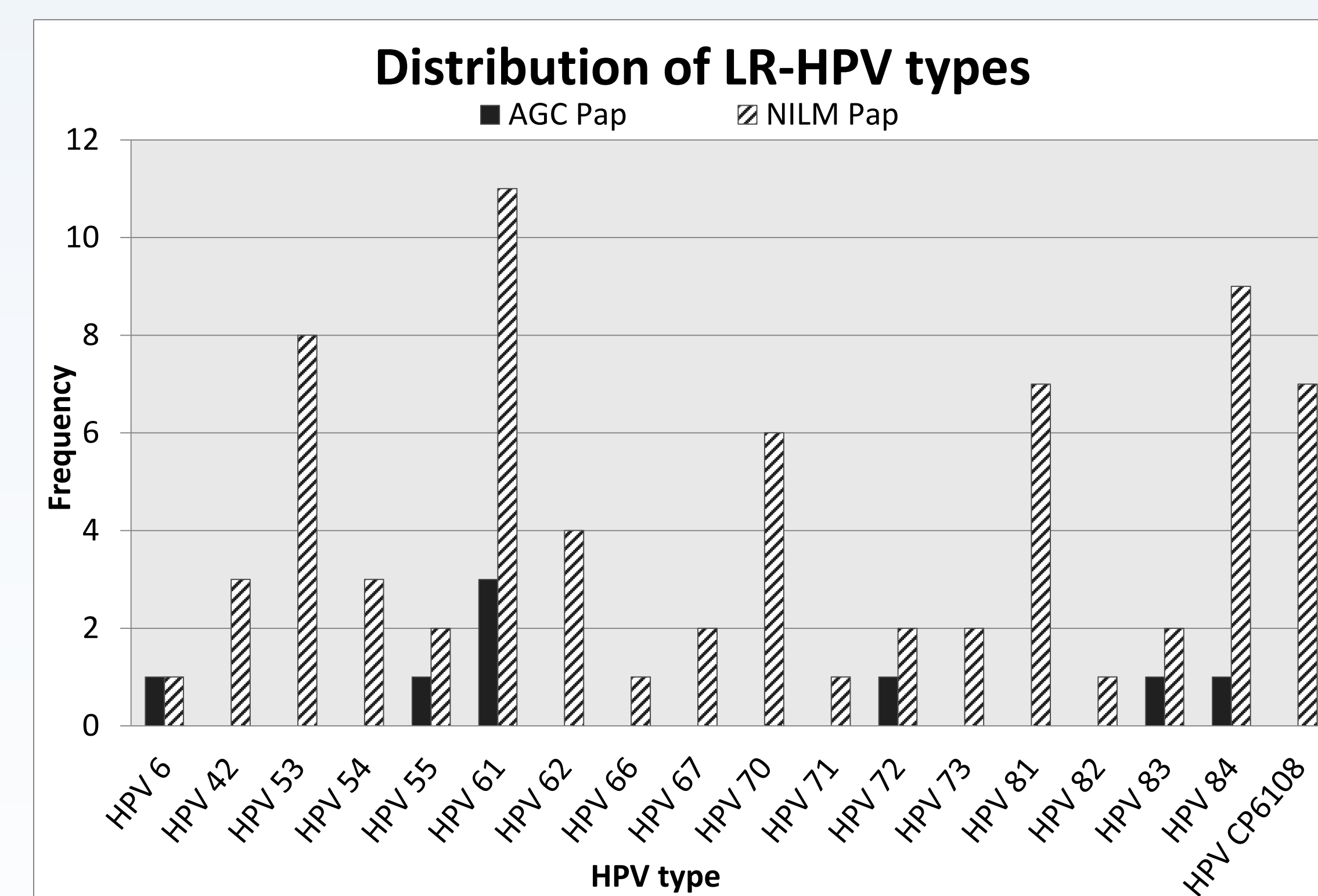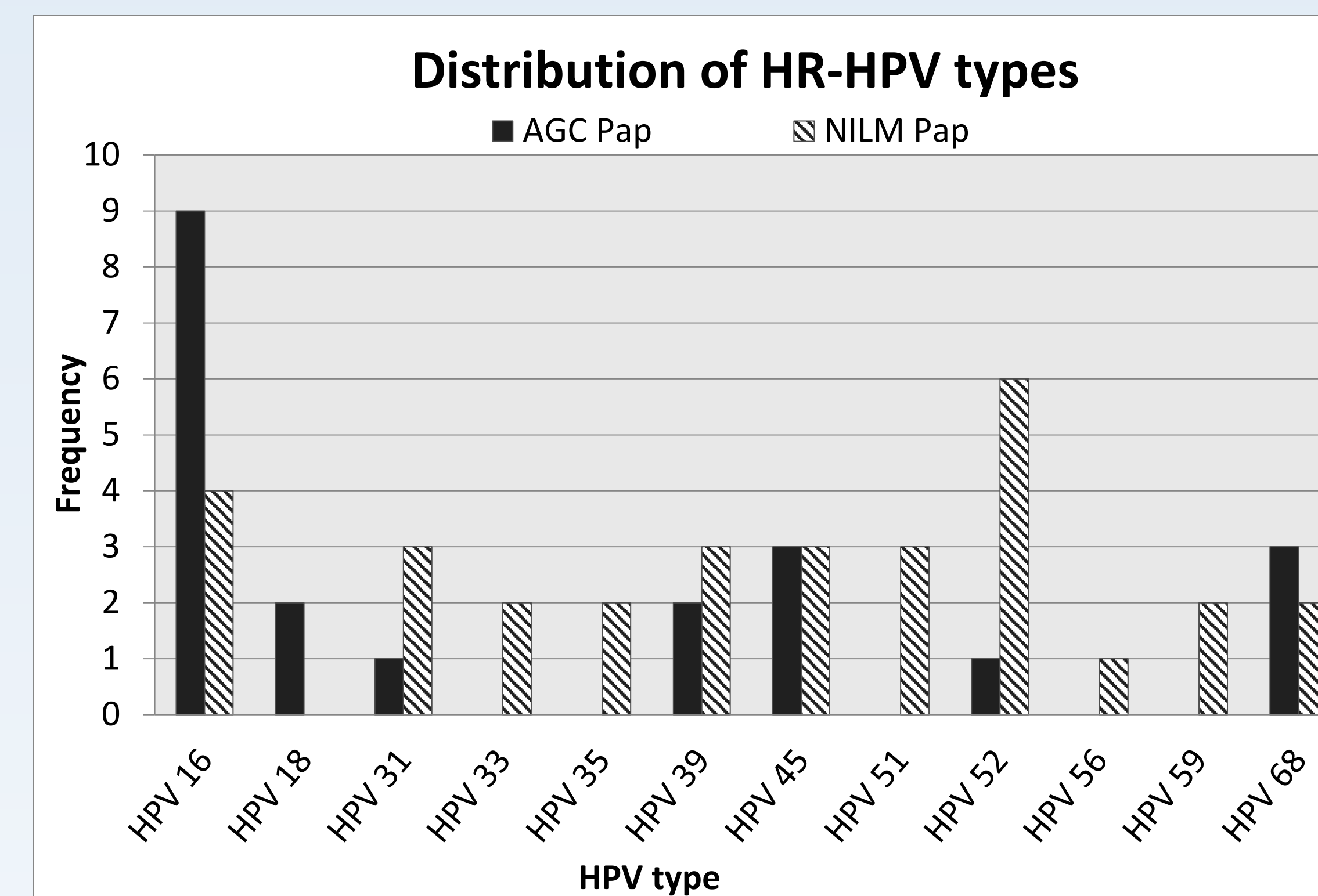
HR-HPV types: 16, 18, 26, 31, 33, 35 ,39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82
LR-HPV types: 6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 83, 84, IS39, CP6108

Conclusion

- AGC-grade cases contained a significantly higher rate of HR-HPV, especially HPV types 16/18 when compared to NILM controls

- Prevalence of LR-HPV: Not significantly different between cases and controls – suggesting sexual behavior practices similar between both groups e.g. unprotected intercourse

- Most cases (78%) and controls (74%) had single infections

- When multiple HPV types: More common in AGC cases (5.7%) than NILM controls (0.6%)

- Findings support guidelines that HPV testing should be performed on specimens with AGC-grade diagnosis

- HPV 16/18 genotyping may be valuable for managing women with AGC-grade Pap test results

References

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