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Short Birth Intervals and Uterine Cervical Cancer Risk in Jamaican Women

Cathrine Hoyo¹, Kimberly Yarnall¹, and Judith Fortney²

¹ Duke University Medical Center, 347 Hanes House, Box 2914, Durham, North Carolina

² Smailman School of Public Health, Columbia University, New York, NY

Keywords

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High parity, common in developing countries, has been consistently associated with higher cervical cancer (CC) risk. Pregnancy-related immunosuppression has been proposed as a possible mechanism by which oncogenic human papillomavirus (HPV) can replicate [1]. Stanczuck [1] reported a higher risk of CC among women genetically predisposed to lower immune response. *In-vitro* studies also demonstrate increased transcriptional activity of HPV16/18 in a progesterone-rich environment [2]. Indeed, a greater than 2-fold increase in CC risk was reported in women with rapid multiple births [3]. However, this study used nulliparous women as referents, which does not allow one to distinguish the role of parity from that of birth-intervals. Birth-intervals are a modifiable risk factor of CC, 80% of which occurs in developing countries.

To determine whether short birth-intervals increase CC risk, incident cases were identified through the Kingston-St. Andrews, Jamaica, Cancer Registry, and controls were identified from cytology log-books of facilities where cases were diagnosed. Response rates of cases and controls were 82% and 60%, respectively. Analyses are restricted to 183 cases and 214 controls with ≥ 2 pregnancies each lasting ≥ 7 months, (≥ 1 birth interval). The average interval was estimated by dividing the sum of non-pregnant months by total pregnancies. We assessed factors known to be associated with CC or pregnancy for confounding and retained those that changed the OR $\geq 10\%$.

Compared with two births, higher parity was associated with CC risk (adjusted OR=1.81; 95% CI=1.1–3.1 in women with 5+ births). Birth-intervals < 1 year were associated with lower CC risk (OR=0.6; 95% CI: 0.4–0.9). The association was strongest in women with ≥ 4 births (OR=0.4; 95% CI: 0.2–0.8). The significance of these findings remains unclear, because women with shorter intervals had fewer partners – and presumably fewer HPV subtypes -- than women with longer intervals. Progesterone-related HPV-reactivation may be subtype-specific, as some have suggested [4]. Preliminary analyses of Haitian data suggest HPV16/18 is less common than HPV-45, 52 and 58. However, HPV could not be directly evaluated in Jamaica as specimens were degraded due to power outages. Alternatively, pregnancy-related estrogen

Address of corresponding author and for reprint requests: Cathrine Hoyo, Ph.D., Duke University Medical Center, Box 2914 Med. Center, 347 Hanes House, Durham, North Carolina, 27710, Phone: (919) 681-2441, Fax: (919) 684-8675, E-mail: cathrine.hoyo@duke.edu

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surges may increase cervical production of HPV-resistant glandular-endocervical cells such that periods spent pregnant might be protective.

The dose-response trend and direction of the association with established risk factors, parity, cigarette smoking and number of lifetime-sexual partners, suggest these associations are unlikely to be due to chance. Detection bias is unlikely as all cases were asymptomatic at enrollment. To guide CC control in developing countries, it seems prudent to evaluate birth-intervals longitudinally in the context of HPV subtypes, in order to clarify the possible protective aspect of pregnancy.

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Table 1
Adjusted odds ratios for the association of pregnancy intervals and cervical cancer

Average Pregnancy Interval	Cases (n=183) N %	Controls (n=214) N %	Adjusted Odds Ratios *	All subjects (n=397)
Parity = 2				
Less than 12 months	18	30	1.04 (0.5 – 2.4)	48
At least 12 months	25	39	1.00	64
Parity = 3				
Less than 12 months	9	12	0.78 (0.3 – 2.4)	21
At least 12 months	25	31	1.00	56
Parity = 4 +				
Less than 12 months	14	29	0.38 (0.2 – 0.8)	43
At least 12 months	92	73	1.00	165
All parity				
Less than 12 months	41	71	0.58 (0.4–0.9)	112
At least 12 months	142	143	1.00	285

* Adjusted for age, cigarette smoking, age at first coitus and first pregnancy, and socioeconomic status.