Risk of Cervical Dysplasia/Cancer in patients with Inflammatory bowel disease on Immunosuppressants - A Systematic Review and Meta-Analysis

Mythili Menon Pathiyil, MD¹, Vishal Sharma, MBBS, MD, DM², Sebastian Shaji MD, FRCP³, Amy Wilkinson³, Jessica Lisle³

1.Saint Vincent Hospital, Worcester, MA 2. PGIMER, Chandigarh, India 3. Hull University Teaching Hospital, United Kingdom

Introduction

This systematic review and metaanalysis was conducted to determine the risk of cervical abnormalities in patients with inflammatory bowel disease on immunosuppressants and estimate the comparative risk with respect to the general population given that there is conflicting data available on the same.

Methods and Materials

- We searched Embase, Pubmed and Medline for studies that reported rates of cervical intraepithelial neoplasia (CIN), cervical cancer, or high-risk HPV in IBD patients and in controls
- The random effects model was used with inverse variance approach for pooled prevalence and M-H method used for the calculation of relative risk.

Results

- 522 relevant papers were identified from inception to 25th April 2022, out of which 44 titles were selected for full-text screening.
- 9 papers, which included 5 case-control and 4 cohort studies involving 53,781 patients were ultimately included in the quantitative synthesis.
- The pooled prevalence of CIN, cervical cancer and high-risk HPV in the IBD population on immunosuppressants was $0.04 (0.01 0.11, I^2 = 100\%)$.
- Individuals with IBD on immunosuppressants were at a greater risk of cervical dysplasia/cancer when compared with healthy controls (relative risk 3.01, 1.44 6.31, I^2 = 100%).

Study	Experi Events		Events	Control	Risk Ratio	RR	95%-CI	Weight (common)	-
R. L. Goetgebuer et al 2021	56	2098	210	8392	+ 13	1.07	[0.80; 1.43]	3.9%	12.4%
Miao Li et al 2019	4	124	0	372	17	- 26.93	[1.46; 496.63]	0.0%	4.3%
Christine Rungoe et al 2014	1022	27408	2858	1508334	100 mm	19.68	[18.34; 21.12]	4.7%	12.7%
Koczka C.P et al 2013	39	158	21	299	1	3.51	[2.14; 5.76]		12.0%
Marhebian et al 2009	1600	22310	5536	111550		1.45			
CW lees et al 2009	53	362	251	1644	+	0.96	[0.73; 1.26]		12.5%
Huftless et al 2008	10	1165	72	12124	1 1 1	1.45	[0.75; 2.79]		11.5%
Sunanda et al 2008	17	40	8	120		6.37	[2.98; 13.64]		11.2%
Jyothi et al 2006	21	116	6	116	1	3.50	[1.47; 8.35]		10.8%
Common effect model		53781		1642951		2.30	[2.21; 2.40]	100.0%	
Random effects model						3.01	[1.44; 6.31]		100.0%
Heterogeneity: $I^2 = 100\%$, $\tau^2 =$	1.1227, p	0 = 0							
					0.01 0.1 1 10 100				

Discussion

- Individuals with inflammatory bowel disease on immunosuppressants are at an increased risk of developing cervical abnormalities like CIN, cervical cancer, and high-risk HPV lesions as compared to those without IBD.
- These findings point to the importance of undergoing screening at regular intervals and the significance of HPV vaccination in IBD patients in aiding to reduce the risk of developing cervical cancer.
- Given that, gastroenterologists in many patients with IBD often assume the role of the primary care physician, it is important to be aware of the increased risk of cervical cancer in this population and advocate for screening at regular intervals and HPV vaccination in IBD patients.

Contact:

Mythili Menon Pathiyil, PGY 1
Saint Vincent Hospital
mythili.pathiyil@stvincenthospital.com

References:

- 1. Goetgebuer, R. L., Kreijne, J. E., Aitken, C. A., Dijkstra, G., Hoentjen, F., de Boer, N. K., ... & de Vries, A. C. (2021). Increased risk of high-grade cervical neoplasia in women with inflammatory bowel disease: a case-controlled cohort study. Journal of Crohn's and Colitis, 15(9), 1464-1473.
- 2. Allegretti JR, Barnes EL, Cameron A. Are patients with inflammatory bowel disease on chronic immunosuppressive therapy at increased risk of cervical high-grade dysplasia/cancer? A meta-analysis. Inflamm Bowel Dis. 2015 May;21(5):1089-97.

 3. Li, M., Yang, Q. F., Cao, Q., Tang, J., Gao, Y., Zhi, M., ... & Gao, X. (2019). High-risk human papilloma virus infection and cervical neoplasm in female inflammatory bowel disease patients: a cross-sectional study. Gastroenterology Report, 7(5),
- 4. Koczka, C. P., Lukolic, I., Geraldino-Pardilla, L. B., Lee, D. S., & Lawlor, G. (2013). The Association of Inflammatory Bowel Disease and Abnormal Pap Smears in African American Women. Journal of Clinical Gastroenterology, 47(7), 655-656.
- 5. Kane, S., Khatibi, B., & Reddy, D. (2008). Higher incidence of abnormal Pap smears in women with inflammatory bowel disease. Official journal of the American College of Gastroenterology | ACG, 103(3), 631-636.
- 6. Bhatia, J., Bratcher, J., Korelitz, B., Vakher, K., Mannor, S., Shevchuk, M., ... & Vele, O. (2006). Abnormalities of uterine cervix in women with inflammatory bowel disease. World journal of gastroenterology: WJG, 12(38), 6167.