




# Constipation in Women with High-Grade Intraepithelial Neoplasia and Cervical Cancer: Does the Extent of Cervical Lesion Invasion Influence the Severity of Constipation and Compromise Quality of Life?

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## Abstract

**Introduction** Constipation is a common clinical condition, particularly among cancer patients.

**Objective** To assess the prevalence and severity of CF in women with high-grade intraepithelial neoplasia (HSIL) and cervical cancer (CC), as well as the impact of this condition on their daily lives.

**Methods** A cross-sectional study was conducted at a tertiary cancer center. To assess the presence and severity of constipation, the Rome IV criteria, and the Constipation Scoring System (CSS) were used. To assess the impact of constipation on daily life, the Visual Analogue Scale (VAS) was used.

**Results** The study included 153 patients with HSIL or CC, with a median age of 44 (IQR 35–56) years. Constipation was reported in 54 (35.3%) patients, 33 (61.1%) of those with HSIL, and 21 (38.9%) of those with CC. In constipated patients, the median number of positive Rome IV criteria items was 3 (IQR 2–5). "Irregular or hard stools" was the most common complaint, affecting 41 (75.9%) of the patients. In patients with CC, the use of analgesic medications was associated with constipation ( $p = 0.016$ ). There is no link between constipation and invasive cancer ( $p = 0.492$ ). Constipation had a daily impact of 7.5 (IQR 4.75–9), with no relationship between VAS and clinical diagnosis (HSIL or CC) [7 (IQR 3–9) X 8 (5–9.5),  $p$ -value = 0.536] The more severe the constipation, the more disturbing it is to these women's daily lives.

**Conclusion** Constipation is common in women with cervical lesions, affecting their daily lives regardless of their severity.

## Keywords

- ▶ constipation
- ▶ cervical cancer
- ▶ high-grade intraepithelial neoplasia
- ▶ quality of life

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## Introduction

Cancer is currently regarded as the world's most serious public health problem, accounting for one of the two leading causes of death in people under the age of 70.<sup>1</sup> In Brazil, 17,010 new cases of cervical cancer (CC) were expected in 2023.<sup>2</sup> In turn, the incidence of cervical high-grade squamous intraepithelial lesions (HSIL), before stabilizing, decreased for several years.<sup>3</sup>

Constipation affects 10% to 15% of adults in western society, with some studies indicating a higher prevalence in women, the elderly, and non-white populations.<sup>4</sup> Cancer patients are more likely to experience constipation, especially in the later stages of the disease.<sup>5,6</sup> Furthermore, intestinal dysfunction can reduce the quality of life of patients, and this impairment is particularly significant in the domains of general health, social functioning, and mental health.<sup>6-8</sup>

For tumors at an early stage, local excision (conization) with free margins, simple hysterectomy, or radical surgery with adjuvant treatment may be necessary, depending on the stage and risk factors, while chemoradiation is generally applied for locally advanced cervical cancer.<sup>9,10</sup> Pelvic surgery and radiotherapy are commonly linked to secondary pelvic organ disorders, which frequently result in post-treatment urinary, intestinal, and sexual dysfunction.<sup>11,12</sup> Furthermore, most cancer patients will feel pain at some point, with 59% of patients undergoing anti-cancer treatment experiencing this symptom, which is usually moderate or severe in intensity.<sup>13</sup> In this regard, pain treatment, particularly when opioids are used, has an adverse impact on intestinal function.<sup>14</sup>

As a result, the purpose of this research is to determine the frequency and severity of CF in women with HSIL and CC, as well as to describe the signs, symptoms, and factors that are most associated with this intestinal dysfunction. The impact of CF on these women's daily lives will be investigated, with a focus on the impact of the severity of the cervical injury on this aspect of their lives.

## Methods

### Study Design and Population.

This is an observational, cross-sectional study with a sample of women with HSIL and CC who attended a public cancer center, in Salvador – Bahia – Brazil. Data was collected from October 2022 to May 2023.

Women aged 18 years or older with HSIL or CC, whether treated or not, who were willing to participate in the research and agreed to the informed consent form were included. Women who were illiterate or semi-literate, as well as those with gastrointestinal anatomical or neurological malformations, were excluded.

Structured electronic forms (Google Forms) were used to collect data. The Rome IV Criteria were used to assess constipation, and a woman with two or more positive items was considered constipated.<sup>15</sup> The Constipation Scoring System (CSS) adapted, and validated for the Portuguese language was used to assess constipation intensity.<sup>16</sup> A

self-report questionnaire was used in addition to the aforementioned instruments to collect information about demographic characteristics (age), education, painkiller use, and childbirth (number of pregnancies and type of birth). The Visual Analogue Scale (VAS) was used to assess the impact of constipation on women's daily lives.

Data were collected on an outpatient basis, in a private room, with questions answered individually and privately, with no interference from the researcher, who only assisted in the process when requested by the interviewee, ensuring the confidentiality and security of the information. Participants completed the form using their own cell phones or readily available computers after receiving the form link via message or email and signing the informed consent form. The research team had no prior contact with the women. All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committees (no. 65595922.6.0000.5544) and with the 1964 Helsinki Declaration and its later amendments.

### Statistical Analysis

The Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, EUA), version 14 for Windows, was used for database development and descriptive/analytical analysis. After normality testing with the Kolmogorov-Smirnoff test, categorical variables were expressed as absolute frequencies and percentages, while continuous variables were expressed as medians and interquartile intervals (IQR).

The Mann-Whitney U test was used to assess the relationship between numerical and categorical variables. The chi-square test was used to assess the relationship between the categorical variables. The Spearman's Correlation Coefficient was used to examine the relationship between the numerical variables. The statistically significant level was defined as a p-value of 0.05.

## Results

### Characterization of the Sample

Study participants included 153 patients with HSIL and CC; their median age was 44 (IQR 35–56) years, and 73 (59.3%) had not finished high school. In relation to previous pregnancies, the majority (129–89%) had already experienced childbirth, with a median of 2 (IQR 1–3) births, and the majority (115–79.3%) had vaginal deliveries. (► **Table 1**). In terms of diagnosis, 99 (64.7%) of the women had HSIL, while 54 (35.3%) had CC. According to IFGO,<sup>17</sup> many patients with CC have locally advanced cervical cancer. (► **Table 2**)

In terms of the therapeutic approach applied, the Loop Electrosurgery Excision Procedure (LEEP) was selected as the predominant method (N = 98, 99%) for women diagnosed with HSIL. In turn, the majority (38–70.4%) of women with CC had already undergone quimioradiation.

Regarding age, patients with HSIL were younger when compared to patients diagnosed with CC [43 (IQR 32–52) x 49 (IQR 37–61.25), p = 0.001]. Many patients with CC required some analgesic therapy (p < 0.001). (► **Table 3**)

**Table 1** Sample description – sociodemographic data

Variable	Patients N = 153
Ethnicity N (%)	
Brown	71 (58,2)
Black	38 (31,1)
White	10 (8,2)
Indigenous	1 (0,8)
Asian	2 (1,6)
Schooling N (%)	
Incomplete High School or less	73 (59,3)
Complete High School or more	50 (40,7)
Age years (ME/IQR)	44 (35-56)
Previous Childbirth N (%)	129 (89)
Type of Childbirth	
Vaginal	115 (79,3)
Cesarean	39 (26,9)
Number of Childbirths (ME/IIQ)	2 (1-3)

Abbreviations: IQR, interquartile range; ME, median; N, number.

**Table 2** Staging of women diagnosed with invasive cervical carcinoma according to the FIGO

Variables	Patients N = 54
Staging N (%)	
1B	6 (11,1)
2A	7 (13)
2B	11 (20,4)
3A	10 (18,5)
3B	8 (14,8)
3C	3 (5,6)
4A	4 (7,4)
Undefined staging	5 (9,3)

Abbreviations: FIGO, *International Federation of Gynecology and Obstetrics*; N, number.

### Constipation Analysis

The analysis of constipation revealed that 54 (35.3%) of the patients were constipated. There was no difference in socio-demographic variables, number or type of birth, or diagnosis (HSIL/CC) between constipated and non-constipated patients. Conversely, non-constipated women used analgesic medications less frequently than constipated women [22 (22.2%) X 22 (40.7%),  $p=0.016$ ], even though the specific classes of such medications were not identified. (► **Table 4**)

The median number of positive items in the Rome IV Criteria among constipated patients was 3 (IQR 2-5), and there was no significant difference between constipated patients with HSIL and CC [3 (IQR 2-5) X 3 (IQR 2-4);  $p=0.805$ ]. The most common symptom was the presence

**Table 3** Comparison between patients with HSIL and CC according to clinical and demographic variables

Variables	HSIL N = 99	CC N = 54	p value
Age (ME/IQR)	43 (32-52)	49 (37-61,25)	0,001*
Number of Childbirths (ME/IQR)	2 (1-3)	2,5 (1,25-4)	0,11*
Type of childbirth N (%)			
Vaginal	74 (76,3)	41 (85,4)	0,202**
Cesarean	25 (25,8)	14 (29,2)	0,665**
Painkiller N (%)	4 (4)	40 (74,1)	< 0,001**

Abbreviations: CC, cervical cancer; HSIL, high-grade intraepithelial neoplasia; IQR, interquartile; ME, median; N, number.

\*Mann-Whitney test; \*\* Chi-square test.

of "irregular or hard stools," which occurred in 41 (75.9%) women (► **Table 5**).

When assessing the severity of constipation, the median CSS present in constipated patients was 10 (IQR 8-14) points, and there was no significant difference between patients with HSIL and CC [10 (IQR 9-13) X 11(IQR 7.5-15.25);  $p=0.385$ ]. ► **Table 6** displays the frequency of CSS items, revealing that many women (32-71.1%) had constipation for more than 20 years.

### Impact of Constipation on the Daily Lives of Constipated Women

Most of the constipated women (57.4%) had a VAS score greater than 7. The median VAS score for constipated patients was 7.5 (IQR 4.75-9.00) There was no relationship between the VAS score and the diagnosis of the cervical lesion (HSIL or CC) [7 (IQR 3-9) X 8 (5-9.5),  $p\text{-value}=0.536$ ] when researchers looked at the impact of constipation on the daily lives of constipated women. However, both groups had a VAS score of 7, indicating that the presence of constipation, regardless of the severity of the cervix lesion, hampered these women's daily lives.

Furthermore, a strong positive relationship was found between "impact on daily life" and "number of positive items in Rome IV" (Spearman Correlation Coefficient = 0.783,  $p\text{-value} < 0.001$ ). As a result, as the severity of CF increased, more severe cases of constipation caused a greater impairment in quality of life. (► **Fig. 1**).

Similarly, there was a strong positive correlation between the CSS score and the impact of constipation on daily life as measured by the VAS (Spearman coefficient = 0.897,  $p\text{-value} < 0.001$ ). As a result, as the CSS score rises, so does the perception of impairment in daily life. (► **Fig. 2**)

### Discussion

The present study found a prevalence of constipation of 35.3% in women with cervical lesions, regardless of

**Table 4** Association between constipation and sociodemographic/clinical variables

Variables	Absent Constipation N= 99	Present Constipation N= 54	p value
Age (ME/IQR)	44 (33 - 57)	46,5 (36 - 53,75)	0,731*
Clinical Diagnoses N (%)			0,492**
HSIL	66 (66,7)	33 (33,3)	
CC	33 (61,1)	21 (38,9)	
Painkiller	10 (10,1)	13 (24,1)	0,021**
Number of childbirths (ME/IQR)	2 (1-3)	2 (1- 4,75)	0,173*
Scholling (%) Until Elementary school	38 (48,7)	26 (57,8)	0,671**
≥ Greater than high school	40 (51,3)	19 (42,2)	
Type of childbirth N (%)			
Vaginal	69 (74,2)	46 (88,5)	0,042**
Cesarean	26 (28)	13 (25)	0,700**

Abbreviations: IQR: interquartile; ME: median; N: number.

\*Mann-Whitney test; \*\* Chi-square test.

**Table 5** Frequency of signs and symptoms comprising the Rome IV criteria in constipated patients

Variables	Patients N= 54
Number of positive Rome IV items (ME/IQR) Roma IV Criteria	3(2-5)
Manual maneuvers to facilitate stool passage	11 (20,4)
Decreased bowel frequency	34 (63)
Irregular or hard stools	41(75,9)
Straining during bowel movements	33(61,1)
Sensation of incomplete evacuation	33(61,1)
Feeling of obstruction or blockage	33(61,1)

Abbreviations: IQR, interquartile range; ME, median; N, number.

the degree of invasion. In turn, many constipated patients with CC used analgesic medication. Concerning the impact of constipation on these women's daily lives, constipated patients showed significant impairment of quality of life measured by VAS, with this effect occurring regardless of whether the lesion was invasive or not.

The study found a high prevalence of constipation, despite the fact that the literature suggests a lower prevalence in the general population, ranging from 15 to 20%.<sup>4,18,19</sup> Nevertheless, it is crucial to emphasize that previous research indicates an elevated prevalence of constipation among cancer patients, with rates ranging from 30 to 60%.<sup>6,20</sup> The high prevalence can be attributed to the frequent use of analgesic medications, specifically opioids, among these patients. Opioids are frequently prescribed medications for alleviating intense pain, a prevalent issue among cancer patients. However, constipation is a frequently encountered side effect of these medications.<sup>6,7</sup> This group of drugs often leads to constipation by changing receptors in the enteric nervous

system. This creates a unique type of constipation called opioid-induced constipation, which usually needs a different treatment method.<sup>6,7</sup> While we noticed that constipated patients with CC consumed a higher quantity of analgesic medications, we were unable to identify the specific type of medication due to many patients being unable to provide us with this information. Nevertheless, there was no discernible disparity in the prevalence of constipation between patients diagnosed with CC and those diagnosed with HSIL. Therefore, we infer that the occurrence of this issue in patients with more invasive lesions is attributable to the analgesics they were administered, potentially opioids, rather than the tumors themselves. Furthermore, the symptoms and signs most reported by our sample ("hard or irregular stools" and "3 or fewer bowel movements per week") bring us back to the use of such medications, in contrast to complaints of the need for manual maneuvers and the sensation of incomplete evacuation or defecation obstruction, which are more commonly associated with the presence of defecatory disorders. It is crucial to emphasize that most women in the study had HSIL, which is a non-invasive lesion that can result in milder pain compared to CC. Hence, the constipation experienced by these women may be attributed to additional factors, specifically inadequate nutrition, since the relatively milder pain could have been alleviated with non-opioid analgesics. Moreover, many women experienced chronic constipation, indicating that intestinal dysfunction occurred prior to the development of the cervical lesion.

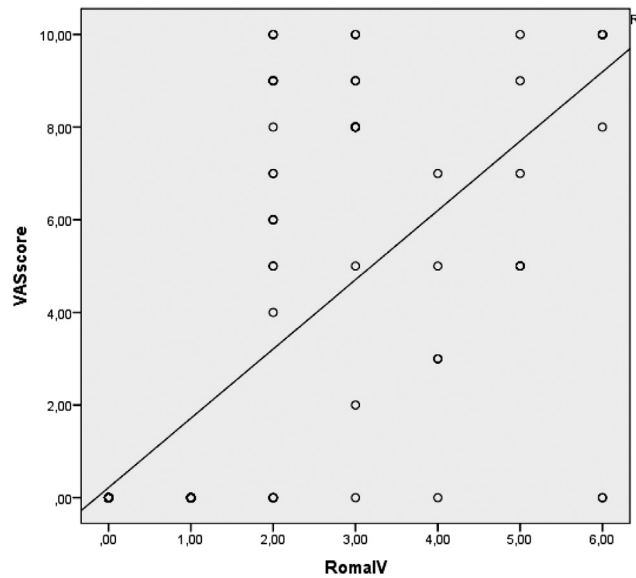
In comparison to multiple-item questionnaires, the impact of constipation was assessed using the VAS, an instrument with good validity and excellent reliability that is simple to understand in a variety of populations.<sup>21,22</sup> Because most of our patients had a low level of education, VAS could have been especially useful in our evaluation. As a result, the use of this simple instrument may have reflected the patient's true perception. In this study, we discovered

**Table 6** Intensity of constipation and frequency of signs and symptoms in constipated women according to CSS

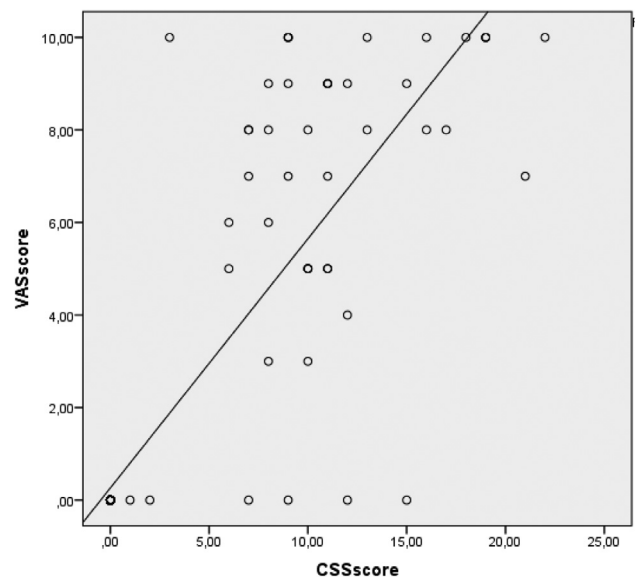
Variables	Patients N = 54
CSS score (ME/IQR)	10 (8-14)
Bowel Movement Frequency N (%)	
1 to 2 times every 1 or 2 days	17 (37,8)
2 times a week or less	28 (62,2)
Straining Frequency N (%)	
Never	10 (22,2)
Rarely	3 (6,7)
Frequently	32 (71,1)
Incomplete Bowel Movement Frequency N (%)	
Never	10 (22,2)
Rarely	1 (2,2)
Frequently	34 (75,6)
Average Time Spent per Bowel Movement Attempt N (%)	
Less than 5 minutes	15 (33,3)
Between 5 and 10 minutes	15 (33,3)
More than 10 minutes	15 (33,4)
Need for Assistance with Bowel Movements N (%)	
None	33 (70,2)
Stimulant laxative	5 (10,6)
Digital assistance or enema	9 (19,1)
Number of Unsuccessful Bowel Movement Attempts in 24 Hours N (%)	
None	23 (51,1)
1 to 3 attempts	19 (42,2)
3 to 6 attempts	1 (2,2)
6 to 9 attempts	2 (4,4)
Duration of Constipation N (%)	
Less than 1 year	3 (6,7)
1 to 5 years	6 (13,3)
5 to 10 years	2 (4,4)
10 to 20 years	2 (4,4)
More than 20 years	32 (71,1)

Abbreviations: CSS, Constipation Scoring System; IQR, interquartile range; ME, median; N, number.

that whether CC was present, there was a significant reduction in quality of life. This suggests that, regardless of the severity of the tumors, constipation is a dysfunction that already has an impact on patient's daily lives and should be addressed and managed appropriately by any specialty, not just a specialized center. Furthermore, many patients (32-71.1%) have had the condition for more than 20 years, highlighting the multifactorial nature of constipation, which



**Fig. 1** Correlation between number of positive items in Rome IV and VAS score VAS = visual analogue scale.



**Fig. 2** Correlation between CSS and VAS Score CSS = Constipation Scoring System; VAS – Visual analogue score.

is linked to a variety of other factors such as diet, poor lifestyle habits, and the use of certain medications<sup>6</sup>.

The CSS, a questionnaire that provides information about the severity and duration of the intestinal condition, was also used to better assess constipation. The sample of constipated patients had a median score of 10 (IQR 8–14), and there was no significant difference between patients with HSIL and CC, reinforcing the hypothesis that the occurrence and severity of constipation are unrelated to the invasiveness of the cancer. A strong positive relationship (Spearman Correlation Coefficient = 0.783) was found between the variables "number of positive Rome IV items" and "impact of constipation on daily life." This shows that intestinal dysfunction, especially the more severe symptoms, makes these women's daily lives harder. As a result, we should not underestimate or postpone

the approach to constipation because early and effective treatment can promote changes in quality of life, with scores improving after relief of this symptom.

It is important to note that the use of the VAS instead of a validated questionnaire to measure quality of life can be questioned as a study limitation. However, by employing the VAS, a simpler and more direct assessment method, including the detection of constipation,<sup>14</sup> this assessment may have aided patient comprehension, as many of the patients have a low educational level. Because constipation encompasses several signs and symptoms that vary from patient to patient, dividing quality of life into different components, as done in some questionnaires, could compromise the analysis of the syndrome's overall impact.<sup>8,23,24</sup> Furthermore, our study was carried out exclusively in a public health center, thus limiting its ability to accurately represent the general population. Finally, because the vast majority (99.3%) of the women had already received treatment, the study was unable to assess associations between the treatments used and the presence of constipation.

## Conclusion

As a result, regardless of the extent of invasion, constipation is a common dysfunction among women with cervical lesions, lowering their quality of life. Constipation is thus a clinical condition that should not be underestimated and should also be addressed by non-specialists.

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None.

**Conflict of Interest**  
None.

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