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*Research Article*

# Prevalence of Pregnancy Outcomes among Reproductive Age Women Following Cervical Intraepithelial Neoplasia Treatment in Zambia

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## ABSTRACT

**Background:** This study determined the prevalence of pregnancy outcomes among reproductive-age women following Cervical Intraepithelial neoplasia treatment in Zambia.

**Methods:** In this descriptive study, prevalence was estimated using records of 8,000 women ages of 15 and 49 who received treatment for cervical intraepithelial neoplasia at the Adult Infectious Disease Control Centre between January 2010 and December 2020 or were human papilloma virus negative after visual inspection acetic acid. STATA version 16 was used to analyze the data. Descriptive analysis determined the frequency distribution and estimated the prevalence of the desired outcomes. The associations were established at 95% confidence intervals by Fisher's exact test and chi-square analysis.

**Results:** Overall, across the two groups combined, 28% of the respondents developed adverse pregnancy outcomes. Normal pregnancy outcomes were less in the treated group (60.8% vs 83.1%) after determining prevalence for each group. The treated group had a higher prevalence of abortions (19.6% vs. 6.7%) and prolonged labor (16.5% vs. 6.3%) compared to the untreated group. In comparison, the untreated group accounted for a higher prevalence of prematurity, 108 (2.7% vs 3.1%), and stillbirths, 18 (0.5% vs 0.9). Thermal ablation accounted for the majority of APOs (82%), LEEP (49.9%), and Cryotherapy (16.1%).

**Conclusions:** The prevalence of adverse pregnancy outcomes was high. The common adverse pregnancy outcomes were abortion and prolonged labor. Treatments like cryotherapy, thermal ablation, and LEEP may affect cervical integrity differently, leading to varied pregnancy outcomes. Recognizing the increased risk of APOs associated with CIN treatment could significantly influence clinical practices related to colposcopy and antenatal care.

## Keywords

Prevalence, Pregnancy Outcomes, Cervical Intraepithelial Neoplasia, Cryotherapy, Thermal Ablation, Loop Electrosurgical Excision Procedure, Reproductive Age Women.

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## Background

Cervical treatments are standard procedures for treating cervical dysplasia, especially among women of reproductive age who may plan to have future pregnancies [1]. In Zambia, the typical Cervical intraepithelial neoplasia (CIN) treatment methods include thermal ablation, cryotherapy, and the loop electrosurgical excision procedure (LEEP) [2]. While the goal of treatment is to remove precancerous tissue while maintaining cervical function,

research suggests that prior treatment may elevate the risk of adverse pregnancy outcomes (APOs) in future pregnancies [3]. In the Sub-Saharan region, Zambia has some of the highest maternal and perinatal mortality rates. It is crucial to prioritize recognizing and addressing avoidable treatments that significantly impact the prevalence of pregnancy outcomes, including considering alternative options when designing and implementing intervention programs. Given these concerns and reported prevalence [4], it is crucial to ensure that additional treatments, such as CIN treatment, do not contribute to the rising statistics, thereby improving care for women and newborns. This study is unique as it presents the combined overall prevalence of APOs between the two groups, encompassing four different pregnancy outcomes within the same population and report. The APOs of interest previously published in a pilot study prior to this study [5] were abortion, prematurity, stillbirths, and prolonged labor. This study determined the prevalence of adverse pregnancy outcomes among the treated and untreated reproductive-age women following Cryotherapy, Thermal Ablation, and Loop Electrosurgical Excision Procedure treatments in Zambia.

## Methods

This cross-sectional study employed a descriptive design using a record review to estimate the prevalence of pregnancy outcomes among 8,000 women aged 15-49. Data collection occurred from February 2023 to August 2023 at the Adult Infectious Disease Control Centre using records from January 2010 and December 2020. The participants were divided into two groups: those who received CIN treatment after VIA screening (n=4,000) and those screened for VIA (n=4,000) only. Women meeting the criteria were identified using VIA screening and CIN treatment records. Respondents were included if they had conceived after undergoing VIA screening or CIN treatments. For the treated group, women met the inclusion criteria if they confirmed experiencing an APO after any cryotherapy, thermal ablatio or LEEP treatments. For the comparison group, women met the inclusion criteria if they were screened with VIA and tested negative for HPV. After the respondents gave verbal consent to participate in the study, data was extracted and collected by the researcher and five trained oncology nurses trained in VIA screening and treatment using a telephone survey and a structured questionnaire to gather data on APOs following CIN treatments and VIA. The questionnaire included both yes/no and continuous response options. The sample size was calculated using the formula for comparing two proportions [5,6]. Census sampling was applied to select the records. For respondents who received single CIN treatment, the first birth following the excision was considered; for those with multiple treatments, the birth following the most recent procedure was used. Data were directly entered into Stata version 16 on a secure, password-protected laptop. To maintain privacy, personal identifiers were removed and replaced with research numbers. The data were verified, cleaned, and analyzed using STATA version 16. Descriptive statistics were used to determine APO prevalence and frequency distribution within the study population. Associations were tested using Chi-square and Fisher's exact tests with a 95% confidence interval, and all tests were conducted at a 5% significance level.

## Results

### Baseline Characteristics

**Table 1:** Socio-demographic characteristics between treatment groups (n=8000).

| Characteristic | Levels | Treatment group | | Total n (%) |
|---|---|---|---|---|
| | | Treated = 4,000 n (%) | Untreated = 4,000 n (%) | |
| Age | < 20 years | 574 (14.4) | 39 (0.97) | 613 (7.7) |
| | 20 – 30 years | 789 (19.7) | 1,044 (26.1) | 1,833 (22.9) |
| | 31 – 40 years | 2,029 (50.7) | 2,775 (69.4) | 4,804 (60.0) |
| | 41 – 50 years | 608 (15.2) | 142 (3.6) | 750 (9.4) |
| Age at delivery | < 20 years | 187 (4.7) | 50 (1.3) | 237 (3.0) |
| | 20 – 30 years | 1,500 (37.5) | 1,548 (37.8) | 3,048 (38.1) |
| | 31 – 40 years | 2,165 (54.1) | 2,299 (57.5) | 4,464 (55.8) |
| | 41 – 50 years | 148 (3.7) | 103 (2.6) | 251 (3.1) |
| Level of education | Primary | 1,394 (34.9) | 319 (8.0) | 1,713 (21.4) |
| | Secondary | 1,021 (25.5) | 1,422 (35.6) | 2,443 (30.5) |
| | Tertiary | 1,585 (39.6) | 2,259 (56.5) | 3,844 (48.1) |
| Socio-economic status | Upper middle | 1,717 (42.9) | 2,118 (52.9) | 3,835 (47.9) |
| | Lower middle | 891 (22.3) | 1,198 (30.0) | 2,089 (26.1) |
| | Other | 1,392 (34.8) | 684 (17.1) | 2,076 (26.0) |

Most respondents were aged 31–40 years (60%; n=800) and 20–30 years (22.9%; n=8000), and the majority were in the same age groups (20-30 and 31-40) at delivery. About, (48.1%) of the respondents attained secondary-level education, and 47.9% and 26.1% were in the upper and lower middle economic class, respectively (Table 1).

Overall, the two groups combined (28%) of the respondents experienced adverse pregnancy outcomes. Abortions of 1,050 (46.8%), prolonged labor of 909 (40.5%), and prematurity of 230 (10.3%) accounted for the majority of adverse outcomes among respondents who experienced adverse outcomes (Figure 1).

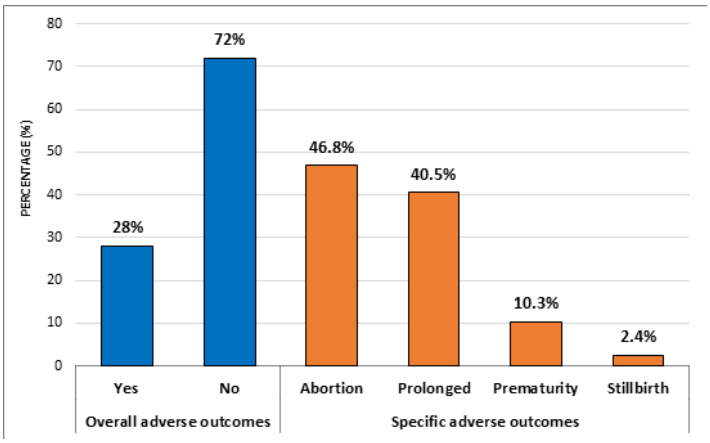


**Figure 1:** Overall prevalence of adverse pregnancy outcomes (n=8000).

Figure 2 shows that the treated group had a higher prevalence of abortions (19.6%) and prolonged labor (16.5%) compared to the

untreated group. Debatably, the untreated group accounted for a higher prevalence of prematurity, 108 (2.7%), and stillbirths, 18 (0.5%). However, the prevalence of normal pregnancy outcomes (60.8% vs 83.1%) was lower in the treated group relative to the untreated.

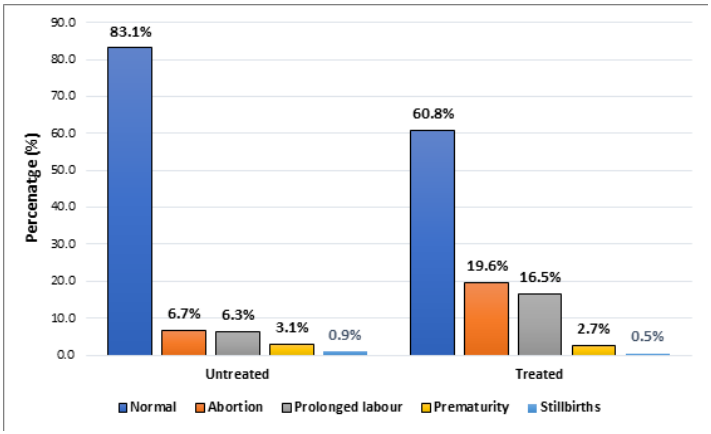


**Figure 2:** Prevalence of adverse pregnancy outcomes between treatment groups (n=8000).

**Table 2:** Pregnancy outcomes across the three levels of treatment (n=8000).

| Outcomes | Overall treatment | | Treatment received | | | p-value |
|---|---|---|---|---|---|---|
| | Yes = 4000 n (%) | No = 4000 n (%) | Cryotherapy n =4000 (%) | Thermal ablation N=4000 (%) | LEEP N=4000 (%) | |
| **Adverse outcomes** | | | | | | |
| No | | | 1,952 (83.9) | 200 (18.0) | 281 (50.1) | |
| Yes | | | 375 (16.1) | 912 (82.0) | 280 (49.9) | **<0.0001**[C] |
| **Total** | | | **2,327 (58)** | **1,112 (28)** | **561 (14)** | |

***LEEP****= Loop Electrosurgical Excision Procedure,* ***C****= Chi-square Test,* ***F****= Fisher's Exact Test*

Thermal ablation (82%) accounted for the majority of APOs, followed by LEEP (49.9) and lastly Cryotherapy (16.1). Cryotherapy was the most common treatment received (58%; n=4000) among the respondents who received CIN treatment.

## Discussion

The study aimed to assess the prevalence of APOs among reproductive age women post CIN screening and treatment. The overall prevalence of APOs was 28% across the two groups. Abortions (46.8%), prolonged labor (40.5%), and prematurity (10.3%) accounted for the majority of adverse outcomes among respondents who experienced adverse outcomes across the 2 groups. This implies that APOs are experienced by both the treated and untreated women. Normal pregnancy outcomes were lower in the treated group (60.8% vs. 83.1%). The treated group experienced a higher prevalence of abortions (19.6%vs 6.7) and prolonged labor (16.5% vs 6.3) compared to the untreated group. However, the prevalence of prematurity (2.7% vs. 3.1) and stillbirths (0.5% vs. 0.9) was lower in the treated relative to the untreated.

The prevalence of APOs in our study was 28%. This is comparable to studies conducted in Ethiopia, North Gondar, and Sub-Saharan Africa, where 28.5%, 28.3%, and 29.7% developed APOs, respectively [7]. However, our findings are higher than those reported in Zambia, Zimbabwe, and Ethiopia, where 18.5%, 15.6%, and 21% developed APOs [5,7,8]. The difference could be the sample size and measurement variables.

The treated group experienced a higher prevalence of APOs, abortions (19.6%), and prolonged labor (16.5%) compared to the untreated group. However, the prevalence of prematurity (2.7%) and stillbirths (0.5%) was lower in the treated relative to the untreated. These results suggest that treatments like cryotherapy, thermal ablation, and LEEP may affect cervical integrity differently, leading to varied pregnancy outcomes. Recognizing the increased risk of APOs associated with CIN treatment could significantly influence clinical practices related to colposcopy and antenatal care. This finding that APOs are more in the treated groups aligns with previous studies [5,7,4]. When comparing the prevalence of APOs between the two groups separately, normal pregnancy outcomes were found to be lower in the treated group (60.8% vs. 83.1%) (Figure 2), which aligns with recent research linking CIN treatment to higher rates of APOs [9,10]. The treated group had a higher prevalence of abortions (19.6%) and prolonged labor (16.5%) compared to the untreated group.

The finding that abortions were more prevalent after CIN treatment is consistent with studies by Sun et al., [11], Zhuang et al., [12], Weinmann et al., [5], who observed an association between pregnancy loss and ablative or surgical treatment and suggested further investigation. This pregnancy loss could result from the procedure reducing the cervical length and elasticity, weakening the compression capacity of the cervix, and reducing the mucus secretion of the cervical glands [13]. However, our finding is different from that reported by Gao et al. [14], which showed the abortion rate after cervical treatment to be consistent with that of the normal population. This result could be different from ours because these outcomes were compared for LEEP treatment only, with a population of 400 with 200 patients in each group, while ours included three treatment types with 4000 patients. Another Cameroonian study by Kenfack et al. [15], reported a 15.2% pregnancy loss and concluded that CIN treatment may not increase the risk of pregnancy loss.

Prolonged labor was another notable APO observed in this study. A plausible explanation for this could be the disruption of cervical tissue and potential scarring resulting from CIN treatment procedures that may affect cervical dilation, leading to difficulties in the progress of labor. This finding is congruent with previous research that reported an increased risk of labor complications, including prolonged labor, following CIN treatment [7,16,17]. The studies further highlighted that the specific treatment received, like cryotherapy, thermal ablation, and LEEP for CIN, significantly influenced the proportion of APOs and may have varying effects on cervical integrity and subsequent pregnancy outcomes [1,17,18]. Still, births were lower in the treated group than in the untreated group. The study by Indarti et al. [19], which showed that CIN

treatment has no association with stillbirths, supports this finding. Our study reported lower prematurity rates, a finding that contrasts with studies by Chigbu et al. [9] and Sun et al. [11], which showed that women with treated CIN had double the odds of giving birth prematurely (before 37 weeks) compared to healthy controls. This finding is different from that of Gao et al. [14], who found a higher incidence of prematurity and reviewed that prematurity was a significant cause of neonatal death and disability and represented an enormous cost to health services and society in general. The explanation why, in the present study, there was no association between CIN treatments and prematurity is well supported by previous studies that did not suggest a difference in the rate of premature delivery after conization compared to the normal population with some results being inconsistent [20]. However, some studies [21,22] indicated that the elevated risk might be linked only to large excisions (10–14 mm, and especially those >15 mm) and that the absence of an association in some studies was due to most women undergoing smaller excisions. In our setting, the excision size was not in the records nor considered in the study. This may inspire future investigations into the potential association mechanism between excision size and premature birth in Zambia. Cryotherapy emerged as the predominant therapy, possibly attributed to its status as the longest-standing treatment for precancerous lesions in Zambia since its introduction in 2006. The finding that thermal ablation increases the prevalence of APOs has not been previously reported and requires further studies.

## Limitations of the Study

We had no information on cone depth, limiting our ability to study the effect of thick excisional cervical surgical procedures on the specific outcomes of interest. This made it impossible to determine which cone size or volume was removed. The respondents with no phones or changed phone numbers did not participate in the study.

## Conclusion

The prevalence of adverse pregnancy outcomes was high. The common adverse pregnancy outcomes were abortion and prolonged labor. Treatments like cryotherapy, thermal ablation, and LEEP may affect cervical integrity differently, leading to varied pregnancy outcomes. These findings highlight the need for careful monitoring and counseling of women who have undergone CIN treatment. Recognizing the increased risk of APOs associated with CIN treatment could significantly influence clinical practices related to colposcopy and antenatal care.


## Acknowledgment

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## Ethical Considerations

The University of Zambia, Biomedical Research Ethics Committee (REF. No. 3185-2022) granted ethical approval, and written permission was sought from the National Health Research Authority (NHRAR-R-1341/08/11/2022).

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