

## Cervical Dysplasias: Experience of the Gynaecology-Obstetrics Department of the Hassan II University Hospital of Fez

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DOI: <https://doi.org/10.36347/sjmcr.2025.v13i01.004>

| Received: 23.11.2024 | Accepted: 27.12.2024 | Published: 02.01.2025

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### Abstract

### Original Research Article

Cervical cancer is a pattern of cancer preceded by a long period of disease at the pre-invasive state, which is characterized on a microscopic level by a broad spectrum events ranging from cellular atypia to varying degrees of dysplasia or neoplasia cervical intraepithelial (CIN), before eventually progressing to invasive cancer. Thus, secondary prevention of cervical cancer is based on screening, diagnosis and treatment of cervical intraepithelial neoplasia, with post-treatment follow-up adequate. **Material and Method:** The objective of our work is to determine the epidemiological profile patients treated for cervical dysplasias, the modalities of diagnosis, the search for the correlation between cytology and histology as well as therapeutic management and monitoring methods. Our study is a retrospective analysis of 58 cases of low- and high-grade CIN, recruited and treated in the Gynecology-Obstetrics II department of the Hassan II University Hospital in Fez, during a period of 04 years from January 2012 to January 2016. **Result:** The average age of our patients was 50.10 years with extremes of 31 and 78 years. Almost all of the patients were multi-gesture (93.10%). 90% of the patients were symptomatic, with symptoms of metrorrhagia in 76% of cases, pelvic pain in 15% of cases and leucorrhoea in 9% of cases. The cytology study by FCV showed a predominance of ASC-H lesions (41.40%), followed by AUC-US (31%), then LSIL (27.60%). Colonoscopic classification a posteriori revealed 62% of TAG2. The histological study on colpo-guided biopsy had shown a predominance of high-grade lesions (CIN2+CIN3) which represented 69% of cases. Low-grade lesions (CIN1) accounted for 31% of cases. Conservative conization therapy was considered in all patients. 49 conizations were performed with a cold scalpel, while only 9 were performed with a diathermic handle. The final histopathological study showed a predominance of high-grade lesions which represented 70% of cases, low-grade lesions represented 17.5% of cases, while cancers represented 12.5% of cases. **Conclusion:** This study allowed us to draw certain specific conclusions on the elements of the diagnosis which are cytology, colposcopy and histology, on the cervical biopsy and on the conization piece, as well as on the therapeutic management.

**Keywords:** Cervical Intraepithelial Neoplasia (CIN), Cervical Dysplasia, Colposcopy, Conization, Cervical Cancer.

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## INTRODUCTION

Cervical cancer is a model of cancer preceded by a long period of pre-invasive disease that is characterized microscopically by a broad spectrum of events ranging from cellular atypia to varying degrees of dysplasia or cervical intraepithelial neoplasia (CIN), before eventually progressing to invasive cancer. Persistent infection of the cervical mucosa with a human papillomavirus is a necessary condition for the development of cervical cancer and its precancerous lesions [2]. If infection with high-risk HPV is necessary, it is insufficient to develop cervical cancer, other sexual and non-sexual factors are involved as cofactors in the progression of infection. Thus, most HPV infections are latent and regress spontaneously without treatment, and only 10 to 15% persist and are responsible for the

development of precancerous lesions and cervical cancer [3]. There is a 10-year period between infection with high-risk HPV and the diagnosis of invasive cancer. This slow evolution makes cervical cancer a pathology that is particularly accessible to screening [3]. Cervical intraepithelial lesions are classified according to the severity of cytological and nuclear abnormalities into low-grade and high-grade lesions. A low-grade cervical intraepithelial neoplasia corresponds to a lesion in which the basal layers include a disorganization of the architecture and cytological atypia that go up to the lower third of the epithelium, the superficial layers contain koilocytes. High-grade lesions are the only abnormalities with the potential to progress to invasive cancer, hence the indication for their management, whereas CIN1 has a very high rate of spontaneous regression, which suggests that these are lesions with a very low potential

**Citation:** Fanfan Mutshe, Fz F'dili Alaoui, A. A. Sanoh, Y. Belhaj, H. Chara, M.A Melhouf. Cervical Dysplasias: Experience of the Gynaecology-Obstetrics Department of the Hassan II University Hospital of Fez. Sch J Med Case Rep, 2025 Jan 13(1): 28-35.

for aggressiveness, calling into question their role as a precursor, hence the indication of their supervision [4]. Primary prevention of cervical cancer is based on prophylactic vaccination against oncogenic types of human papillomavirus, while secondary prevention is based on screening and treatment of cervical intraepithelial lesions.

## MATERIAL AND METHOD

Our study is a retrospective descriptive analysis of 58 cases of patients with cervical intraepithelial lesions treated in the Gynecology and Obstetrics II department of the Hassan II University Hospital of Fez, during a total period of 04 years from January 1, 2012 to January 1, 2016. Patients who presented with a cervicovaginal smear suggestive of high- or low-grade lesions and/or on cervical biopsy, either under colonoscopic control or blinded, an intraepithelial cervical lesion (CIN1, CIN2 or CIN3) were included. In our study, we used patient records, which allowed us to

establish the following exploitation sheet: The results of the FCV The results of the colposcopy are expressed according to the terminology of the French Society of Colposcopy and Cervico-Vaginal Pathology: atypical transformation of grade 1, a or b (TAG1a, TAG1b), or atypical transformation of grade 2, a or b or c (TAG2a, TAG2b, TAG2c). The results of the histological study of the cervical biopsy and the operative specimen are expressed according to the WHO classification in terms of cervical intraepithelial neoplasia (CIN): CIN1, CIN2, CIN3, micro-invasive cancer and invasive cancer. The statistical analysis was performed by SPSS Software version 20.

## RESULT

### Depending on the Frequency:

From 2012 to 2016, 58 cases of cervical intraepithelial neoplasia were treated in our training. The number of patients recruited varied from year to year, with a peak in 2015 (22 cases).

**Table 1: Number of patients per year of recruitment**

Year	2013	2014	2015	2016
Number of case	11	12	22	13
Percentage %	18.96	20.70	37.94	22.40

The average age of our patients was 50.10 years, with age extremes of 31 and 78 years. The most

affected age group was between 40 and 49 years old with a total of 24 cases, or 41.5% of cases.

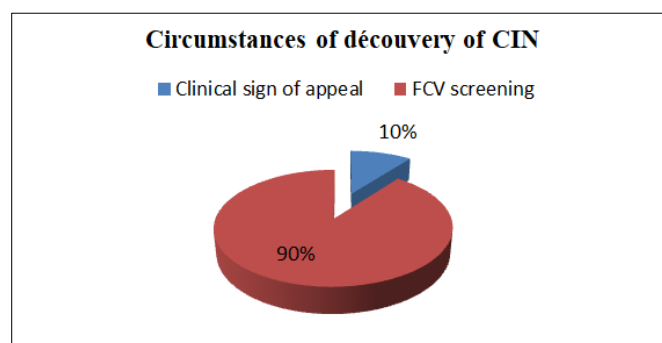
**Table 2: Number of patients by age group**

TSlice of age	≤ à 20 years	20-29 years	30-39 years	40-49 years	50-59 years	≥ à 60 years
Number of patients	0	0	7	24	20	7
Percentage %	0	0	12	41.5	34.5	12

Patients aged 50 to 59 years accounted for 34.5% of cases, or 20 cases in total, while patients aged 30 to 39 years and those over 60 years of age accounted for only 12% of cases, or 7 cases. 46.6% of our patients came from a low socio-economic level. The profession was specified for all patients: 44 were housewives. In our series, 03 patients are nulliparous and 93.1% of our patients were multiparous.

### Circumstances of Discovery:

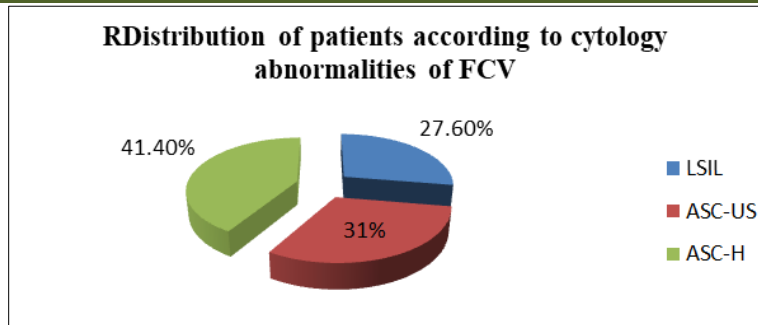
In our series, the discovery of cervical intraepithelial neoplasia was made either: During systematic screening with FCV in asymptomatic patients, 6 cases and during clinical warning signs (52 cases).



**Figure 1: Circumstances of decouvery of CIN**

FCVs were performed either in conventional mode (5% of cases) or in liquid media (12% of cases),

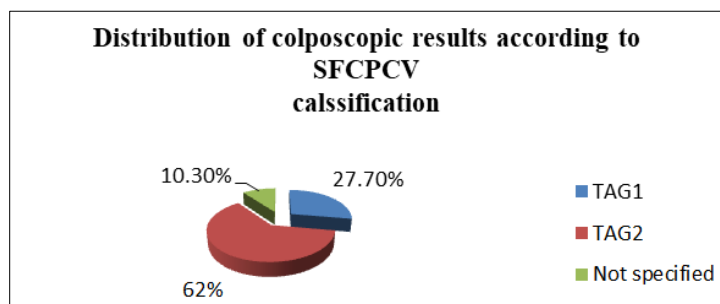
but unfortunately the technique of realization was not specified in 83% of cases.



**Figure 2: Distribution of patients according to cytology abnormalities of FCV**

ASC-H lesions accounted for 41.40% of cases, while LSIL lesions accounted for only 27.60% of cases. We had noted 27.60% of cases of LSIL-type lesions. No Pap smear came back normal, inflammatory or in favor of an HSIL-type lesion. The other abnormalities associated with the above-mentioned noted on FCV were

mainly: stigmata of HPV infection: in 18 cases, glandular dystrophy: in 02 cases, an aspect of cervicitis: in 06 cases. The colposcopy was performed for all our patients, i.e. in 100% of cases. The result of colposcopy was abnormal in 52 cases, or 82.65% of the cases, the results of the remaining 06 cases were not available on the files.



**Figure 3: Distribution of colposcopic results according to the SFCPCV classification.**

**According To the Histological Study of the Biopsy Specimen:**

86.2% of the biopsy specimens were analyzed at the anatomical pathology laboratory of the Hassan II

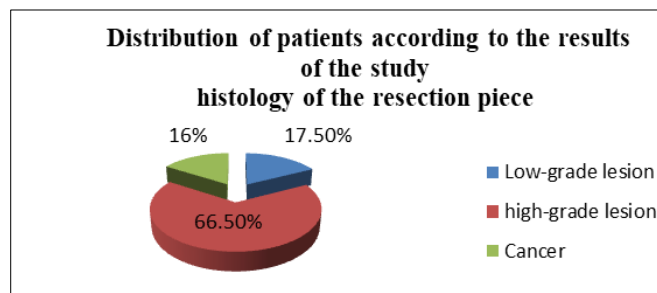
University Hospital in Fez, while the remaining 13.8% were analyzed in laboratories elsewhere. Histology findings were abnormal in all cases.

**Table 3: Distribution of patients according to the result of the histological study of the biopsied fragments**

Histological result		Number of cases	Percentage %
Low-grade lesion	CIN1	18	31
High-grade lesion	CIN2	31	53.4
	CIN3	9	15.5
<b>Total</b>		58	100

49 patients had benefited from a cold scalpel conization, i.e. 84.5% of the cases, only 09 patients had benefited from a diathermic loop resection. 46 surgical specimens were analyzed at the anatomical pathology

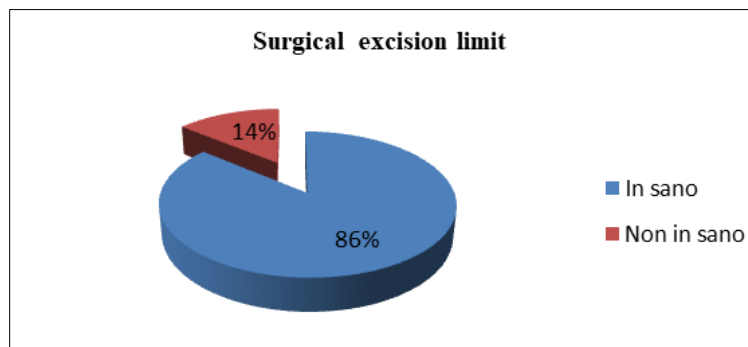
laboratory of the Hassan II University Hospital in Fez, i.e. 79.30% of the cases, while 12 specimens were analyzed elsewhere, i.e. 20.70% of the cases.



**Figure 4: Distribution of patients according to the results of the study histology of the resection piece**

Comparing the results of the biopsy with those of the conization piece, we noticed that they were concordant in 93% of cases (54 cases), and they are discordant in 7% of cases (04 cases). In the case of

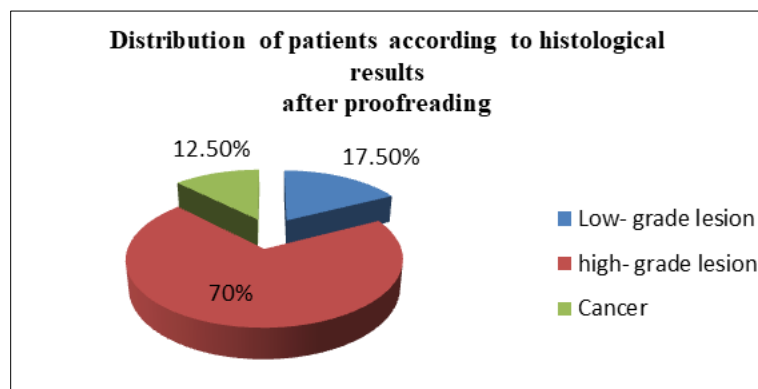
discrepancies, the biopsy underestimated the final lesion in 7% of cases, i.e. in 04 cases. The limits of surgical excision were specified on all histopathological reports.



**Figure 5: Surgical excision limit**

20.70% of the patients had benefited from histological rereading of the resection piece, i.e. 12 cases. All proofreadings were carried out at the anatomical pathology laboratory of the Hassan II University Hospital in Fez. Proofreading was indicated to specify

the limits of resection in 14% of cases (08 cases), and because of the discrepancy between the result of the biopsy and that of the resection specimen in 7% of cases (4 cases).



**Figure 6: Distribution of patients according to histological results after proofreading**

In our series, 04 patients, or 6.5% of the cases, had benefited from revision surgery. In our series, none of the patients had presented an intraoperative complication, there were 03 cases of post-operative cervical stenosis that were subsequently lost to follow-up.

## DISCUSSION

Cervical intraepithelial neoplasia is an asymptomatic lesion. Their incidence and prevalence are difficult to specify because of the imperfect reproducibility of the definition criteria and the inter-observer variations characterizing the modalities of their diagnosis [1, 2]. Recent epidemiological data suggest an increase in the incidence. Andean prevalence of CIN [3, 4], and a decrease in the mean age of patients with the lesion [5]. The annual incidence is five new cases per 1,000 women under 40 years of age and the prevalence ranges from 29 to 65 per 1,000 [6]. Low-grade lesions (condylomas+CIN1) are the most common lesions in

young women [7], while high-grade lesions (CIN2+CIN3) and micro-invasive carcinomas are not uncommon at this age and are often discovered within 2 to 3 years of a normal Pap smear. Conversely, in women over 60 years of age, these lesions are exceptional if the screening smears have always been normal [5].

It appears that the lowest rates, of the order of 0.6%, were noted in the Islamic populations [8], conversely, a prevalence of 20% of CIN was observed in India (8), which represents the highest rate in the literature. The prevalence is 2.63% in South Africa [9], 4.3% in Kenya [10], while rates of 15.6% and 11.7% of CIN have been reported in Zimbabwe and Côte d'Ivoire [11], respectively. However, the comparison of these figures should take into account parameters that are generally unknown or cannot be superimposed, namely: the coverage rate of the population at risk, the methods of patient recruitment (occasional or organized screening) [12]. In Morocco, according to the results of the cancer registry of the greater Casablanca region for

the year 2004, the incidence of cervical cancer is 12.8%. That of intraepithelial neoplasia has not been studied. Our study shows that only 58 cases of intraepithelial neoplasia of the cervix were treated in our training over a period of 04 years (between 2012 and 2016). This figure is not in line with the studies mentioned above, since it is an individual screening of patients who are asymptomatic or who have consulted in the presence of warning signs. Patient recruitment varies from year to year, reaching its peak in 2015 (22 cases) and its minimum in 2013 (11 cases). This reduced number of patients cannot reflect the actual number of women with precancerous lesions. Young age, around the thirties, has been the most reported predisposing factor for CIN in the literature [12]. The average age of onset of lesions increases with their severity. There is a peak in the occurrence of CIN3 between the ages of 25 and 30 [13]. The average age of patients with invasive cancer is 51 years, it occurs on average eight years later than microinvasive carcinoma [13]. In women in the age group between 13 and 22 years, low-grade cytological abnormalities frequently regress and rarely progress, and high-grade cytological abnormalities correspond in only 50% of cases to high-grade neoplasia, mostly CIN2 [14]. This finding is explained by the fact that the incidence of HPV infections decreases with the age of women, while at the same time prevalent HPV infections persist more [15]. As a result, the proportion of older HPV infections increases with the age of women, and given the correlation between the duration of HPV infection and the risk of carcinogenesis, the risk of high-grade neoplasia also increases with the age of patients [16]. A mass screening campaign was carried out in the Rhamnas region (Centre-South of Morocco) by M.-A. Benhmidoune and his team (Department of Hematology Oncology, Mohamed VI University Hospital of Marrakech), involving 861 women whose ages ranged from 17 to 82 years, showed that the 30 to 50 age group was the most affected by intraepithelial cervical lesions (low-grade and high-grade), while no cases were found at extreme ages (less than 20 years and more than 60 years) [17]. In our series, the average age is 50.10 years, with extremes of 31 and 78 years, and the most affected age group is between 40 and 49 years old.

These results cannot be extended in the absence of an organized screening system with good coverage of the population, as well as the often late consultation of our patients in the face of alarming symptoms. The cumulative incidence of HPV infection after the onset of sexual activity is particularly high [16]. All types of HPV combined, the cumulative risk of infection decreases with the age of women: it has been estimated to be between 40 and 80% in the 2 to 5 years after the start of sexual activity in women under 20 years of age, to reach 12.4% after the age of 45 [16]. In our series, none of our patients had benefited from HPV typing. On the other hand, HPV infection, which is controlled by the presence of koilocytes, was present in 46 patients, i.e. in 79% of cases. The determinants of HPV infection in both men

and women are directly related to sexual behavior [18]. The importance of sex life in the epidemiology of cervical cancer has been known since Rigoni Stern in 1842 [19], then it was highlighted for cervical intraepithelial neoplasia (CIN) [19, 20].

Some common criteria relating to sexuality are found in the majority of women with cervical cancer: the early age of first sexual intercourse, the early age of the first pregnancy, the multiplicity of partners, multiparity; Early age of first sexual intercourse: the adolescent cervix is both more exposed to infections and more vulnerable due to: physiological eversion of the glandular mucosa (monolayer epithelium more exposed to breaches allowing the virus to enter), local cellular and humoral immunosuppression in adolescent girls [15]. This makes him very vulnerable to trauma during coitus and childbirth. These traumas facilitate malignant transformations of the cells of the cervix, which are characterized by very rapid cell renewal [21, 22]. A retrospective study at the Ibn Sina University Hospital in Rabat [11], conducted by S. Kessabi and involving 53 cases of patients with high-grade and low-grade intraepithelial cervical lesions recruited over a period of ten years, showed that 11% of these patients had an age of marriage before 16 years of age, 6% between 17 and 20 years old, 9% between 21 and 28 years old, but unfortunately the age of marriage was not specified in 74% of cases. Some studies show that the incidence of infections also increases with the number of partners [15].

Not all women infected with HPV will develop cervical neoplasia and smoking could be a cofactor promoting the appearance of these lesions. Nicotinic derivatives present in cervical mucus are thought to be involved in the dysregulation of the immune response, thus promoting viral replication [23]. Another constituent of smoke, cotinine, is also found in this mucus, even in some non-smoking women, who can be victims of passive smoking [24].

Smoking also increases the risk of lesions progressing. It appears to be another risk factor for recurrence [25], and is significantly associated with the development of invasive cervical cancer. There is a dose effect, moderate smoking multiplies by 3 the risk of the appearance of high-grade lesions, while heavy smoking (more than one pack per day) multiplies it by 4 [21].

In Morocco, and like other developing countries, cervical cancer is second only to breast cancer, and is often diagnosed at an advanced stage. Nevertheless, the incidence of invasive cervical cancer has decreased in developed countries thanks to the generalization and organization of screening activities. The success of screening in general is linked to an organised system with good population coverage, adequate sampling with sensitive and reproducible tests, and the necessary quality controls at all stages [26]. In

our country, there is no organized screening program. Screening is individual, with only one-off campaigns launched by non-governmental organisations (NGOs) working in this field [17]. In countries where screening is organised, the age of start of screening differs from country to country and varies between 20 and 30 years [15]. The sensitivity of cervical cytology to detect high-grade lesions of the cervix is imperfect, varying between about 30 and 80% according to international studies [26]. Thus, the Pap smear only makes sense if it is frequent enough to be able to make up for a false negative at a still favourable stage [25]. We estimate that one to two-thirds of false negatives of cervical cytology are due to improper sampling [26]. Thus, in order to avoid errors that prevent correct interpretation, the sample must comply with the following conditions: the Pap smear should be carried out at a distance from sexual intercourse (48 hours), outside menstrual periods, from any local therapy or infection, and if necessary, after estrogen treatment in postmenopausal women. The vaginal examination before the smear test and the use of lubricant should be avoided, and the cervix should be perfectly exposed with a speculum. Vaginal smear screening or may be associated with other clinical signs that are themselves indicative of predisposing lesions such as metrorrhagia, leucorrhoea, pelvic pain or recurrent cervicitis. In our series, telltale signs were noted in 90% of cases. Colposcopy is the examination of the cervix with a low-magnification stereoscopic binocular loupe with a powerful light source [27]. It allows the cervix to be magnified during visual examination, thus making it possible to identify abnormalities in the mucosa, to specify its topography and to direct biopsies in order to diagnose lesions [16]. In our series, the colposcopic impression was consistent with the histological result obtained by colposcopy-directed cervical biopsy in 77.8% of cases, and which remains Precancerous lesions are asymptomatic and inapparent on speculum examination, they are most often discovered by the cervico-vaginal a percentage similar to the data in the literature which suggest an average percentage between 70 and 90% [28]. Cervical intraepithelial neoplasia is an asymptomatic lesion, its treatment is only justified to prevent its progression to cervical cancer. Low-grade lesions (CIN1) regress spontaneously in more than 60% of cases within 2 years and therefore do not warrant immediate treatment (29). In contrast, high-grade lesions (CIN2+3) have a lower potential for spontaneous regression and put patients at risk of progression to a larger invasive cancer [30]. For these reasons, the diagnosis of a high-grade lesion of the cervix (CIN2 or CIN3) classically requires treatment [31], or by destruction: laser vaporization and cryotherapy or by excision: conization, whether it is performed with a cold scalpel, laser, electric fine tip or loop resection. In our series, 55 patients had benefited from a conization with a cold scalpel, only 3 had benefited from a resection with a diathermic loop. The resection margins were rated as healthy in 100% of cases. No rerecognition was performed in our series, but revision surgery with radical

treatment was performed in 4 patients The post-treatment monitoring strategy adopted by our department is as follows: For low-grade lesions, a colposcopic check-up at 6 months and 1 year followed by annual cytology; For high-grade lesions, a control by cytology and colposcopy at 03 months and then at 06 months after the decision of the specialized staff. In our series, 03 patients have not yet had a check-up, while 2 are excluded from follow-up because they were referred for radiotherapy; For the rest of the patients, they are divided into: good adherence to follow-up: strict compliance with the rhythm of monitoring dictated by the staff's decision: 24 patients. Outcomes were normal in 18 cases, and inflammatory in 6 cases; partial adherence to follow-up: only one check-up performed and then lost to follow-up: 15 patients; this could be attributed to the reassuring result of the first FCV control; for those lost to follow-up: no check-up was carried out: 14 patients. Partial adherence to follow-up could be attributed to the reassuring result of the first control Pap smear: for patients who adhered to a single control and then lost to follow-up, the results of their first control FCVs. No recurrence was noted. The prevention of cervical cancer is organized on two levels: primary prevention: it aims at protection against genital infection by the human papillomavirus and secondary prevention: it is based on the screening, diagnosis and treatment of cervical intraepithelial lesions.

## CONCLUSION

At the end of this work, we can conclude that screening and management of cervical intraepithelial neoplasia is important in the prevention of cervical cancer, which is the 2nd most important cancer in women in terms of incidence and mortality. Through the risk factors studied, we were able to define a profile of exposed women, comparable to that found by several authors. They are young women, of low socio-economic status, multiparous and pre-menopausal in the majority of cases. It is on these women that screenings should preferably focus. The ideal screening test remains the cervicovaginal smear, which must be completed by a colposcopy with directed biopsy to make the diagnosis of CIN. But the cost and lack of availability of these means throughout the country could lead to the preference for other alternatives such as cervical visualization with acetic acid. Colposcopy is the key examination in the diagnosis of high-grade cervical lesions, it allows biopsies to be guided by locating the most suspicious areas, hence the interest in such a simple and precise colonoscopic classification to characterize the colonoscopic pictures and compare them with cytological and histological data. Only treatment of CIN can prevent the further development of invasive cancer, but the possibility of residual lesion or recurrence requires prolonged monitoring. The management of precancerous lesions of the cervix is a cumbersome and expensive procedure, so primary prevention by HPV vaccination remains the best choice of prevention, which is unfortunately not yet widespread in our context.

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