Minireview Article

Cervical Cancer in Burkina Faso: Current Status, Government Strategies, and the Role of Traditional Medicine in Treatment

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ABSTRACT

In Burkina Faso, cervical cancer is the second most common cancer among women, and the second leading cause of cancer-related death. Both incidence and mortality rates have risen steadily in recent years. Its natural history is linked to persistent infection with an oncogenic human papillomavirus, a necessary but not sufficient factor in its development. However, cervical cancer is said to be preventable, due to its slow evolution. To date, it is the only cancer that can be prevented by vaccination against human papillomaviruses (HPV). Systematic and regular screening enables early detection of precancerous lesions so that they can be treated, thereby preventing the onset of cervical cancer. Unfortunately, access to these preventive measures remains limited for the majority of the population due to cost. The government of Burkina Faso, through its Ministry of Health, has put in place strategies to facilitate access to screening and care. Burkina Faso's researchers and teacher-researchers are also collaborating with traditional health practitioners in the search for better remedies and active substances with no side effects, through the use of medicinal plants. This review aims to take stock of cervical cancer in Burkina Faso: achievements, shortcomings, strategies implemented by the government and the contribution of scientific research to the fight against this scourge.

Keywords: cervical cancer, human papillomavirus, screening, medicinal plants, Burkina Faso

1. INTRODUCTION

Cervical cancer is a major public health problem. It is a disease associated with persistent human papillomavirus (HPV) infection [1]. Around 89% of the 565,541 cases of cervical cancer reported worldwide in 2019 occurred in low- and middle-income countries[2]. According to GLOBOCAN estimates, in 2022, in Burkina Faso, 988 new cases of cervical cancer were diagnosed with 775 deaths[3]. Cervical cancer is the second leading cause of cancer mortality among women in Burkina Faso, with a mortality rate of 23.8 per 100,000 women [4]. In Burkina Faso, there is a lack of technical platforms and specialist healthcare staff in our hospital structures, particularly in rural areas, as well as a healthcare system that does not allow regular gynecological screening and care as it does in developed countries [4]. All these factors mean that screening is generally late, resulting in deaths in our countries. These results are all the more worrying given that these deaths are avoidable, and early diagnosis would enable rapid management and therefore cure [5]. Moreover, medical treatment is extremely difficult and expensive; hence its limited accessibility to the vast majority of the population suffering from this cancer [6].

Recent years have seen a surge in therapeutic research into cervical cancer, through the use of local medicinal plants derived from traditional medicine. Indeed, medicinal plants are a source of secondary metabolites with therapeutic properties. Several molecules used in cancer treatment originate from medicinal plants[7], [8]. Several ethnobotanical surveys have been carried out to identify the plants used by traditional practitioners to treat tumours[9]. The aim of this review is to take stock of cervical cancer in Burkina Faso: achievements, shortcomings, strategies implemented by the government and the contribution of scientific research to the fight against this scourge.

2. NATURAL HISTORY OF CERVICAL CANCER

Cervical cancer is a slowly evolving disease of infectious origin, which can take more than fifteen years to develop, from primary infection with an oncogenic human papillomavirus to the various precancerous histological lesions accompanying persistent infection [10]. Human papillomavirus (HPV) infection is a very common sexually transmitted infection[11]. Almost all cervical cancers begin in the epithelium. These cancers can appear either on the outside of the cervix (ectocervix) in 75-80% of cases (squamous cell carcinomas) or on the inside of the cervix (endocervix) in 20-25% of cases (adenocarcinomas) [12].

Persistent infection with high-risk oncogenic HPV (HR HPV) is recognized as the main cause of cervical cancer [1], and HPV infection can disappear (clearance) within a few months. In fact, some 80-90% of HPV infections are transient, disappearing spontaneously within 24 months of first detection [13]. It can also persist for several years (1 to 10 years), progressing to precancerous lesions or cervical intraepithelial neoplasia (CIN), which can be mild, moderate or severe (CIN 1, CIN 2, CIN 3). CIN 3 is a necessary stage for the development of invasive cancer, unlike CIN 1 and CIN 2. Cervical precancerous lesions may regress to normal epithelium, with a probability depending on lesion severity, accompanying viral clearance. They may also persist or progress to a more advanced stage, including CIN 3. The persistence of these lesions leads to the invasion of infected cells and thus to invasive cervical cancer [10].

Rarely, lesions may affect the glandular epithelium of the cervix, corresponding mainly to adenocarcinomas in situ, the only lesion preceding invasion. This lesion, already cancerous, is also due to persistent infection with a high-risk oncogenic HPV.

3. CAUSAL RELATIONSHIP BETWEEN HUMAN PAPILLOMAVIRUS (HPV) AND CERVICAL CANCER

Cervical cancer is caused by many factors. However, the primary and necessary cause is human papillomavirus infection [1]. Human papillomaviruses or HPVs (Human PapillomaVirus) are small (around 60 nm in diameter) naked viruses (without envelopes) of the *Papillomaviridae* family. In 2016, 205 different types of HPV were identified [14]. This virus is common, and the infection it causes is the most frequently diagnosed sexually transmitted infection (STI). The sexual route is the main route of HPV acquisition, although there are other routes [15], [16]. Almost all sexually active women have already been infected with HPV. But in the majority of cases, the infection disappears within six months to two years without symptoms of disease. However, in cases where the infection does not

clear and persists, the likelihood of developing precancerous lesions and subsequent cervical cancer is higher [15]. Precancerous and cancerous lesions of the cervix are caused by so-called high-risk oncogenic HPV types (HR-HPV): HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 [17]. Thus, persistent HR-HPV infection is the cause of nearly 100% of invasive cervical cancer cases, with HPV DNA detected in 90-100% of specimens from cervical lesions [18]. HR-HPVs are responsible for 7.7% of cancers in developing countries (DCs), mainly cervical cancer [19]. HPV types 16 and 18 are responsible for 50-60% and 10-20% respectively of cervical cancer cases encountered in most countries followed by HPV 45 and 31 with 4-8% and 1-5% respectively [18], [20]. Detection of HR-HPV in cervical samples is a highly sensitive tool for identifying women at risk of precancerous or cancerous cervical lesions. The prevalence is just as high in squamous cell carcinomas as in adenocarcinomas, although the distribution of HPV types varies slightly between these 2 histological forms [21]. Indeed, a worldwide study found 90.9% of HPV-positive women with squamous cell carcinoma, compared with 82.0% of those with adenocarcinoma. In contrast, the prevalence of multiple infections did not differ significantly primarily by histological type [22].

4.EPIDEMIOLOGY, RISK FACTORS AND HPV PREVALENCE IN CERVICAL CANCER IN BURKINA FASO

4.1 Epidemiology

Very few data are available on the prevalence, incidence and mortality due to cervical cancer in Burkina Faso due to the absence of a functional cancer registry. Nevertheless, it is estimated to be the second most common cancer (11%) after breast cancer (15.3%) among women. Between 1986 and 2006, it was estimated that cervical cancer accounted for 23% of cancers encountered in women [23]. According to GLOBOCAN data, cervical cancer represents 6.8 % of all cancers cases diagnosed in 2022 in Burkina Faso [3]. In 2022, 988 cases of cervical cancer were recorded with 775 deaths, which is 78.4% of diagnosed cases [3]. This shows that cervical cancer is a major public health problem in Burkina Faso.

4.2 Risk factors

Although HR-HPV infection is necessary, it is not sufficient to induce precancerous or cancerous lesions. This infection must persist for several years to lead to the appearance of precancerous lesions, and this persistence can be influenced by several factors [1]. These include environmental factors, use of oral contraceptives, co-infections (with HIV or several HPV types, for example) that weaken the immune system, smoking, frequency of re-infections...[24]. There are very few data on association between these different factors and the occurrence of cervical cancer in Burkina Faso. However, a study found a significant association (p=0.01) between the number ofpregnancies and the occurrence of precancerous lesions and cervical cancer [25]. Another study on precancerous lesions found association between malphigian intraepithelial lesions of the cervix, HIV 1 co-infection and HPV multiple infection positivity [26]. Other cofactors such as age at first intercourse, smoking and the presence of other sexually transmitted infections were not associated with precancerous cervical lesions in this study[26]. In addition, some of these factors increase the risk of HPV infection, and therefore promote the development of cervical cancer. In Burkina Faso, these are: age, age at first sexual intercourse, marital status, level of education, occupation, number of sexual partners, frequency of sexual intercourse, non-use of condoms and history of sexually transmitted infections, use of contraceptives, HIV infection [27]–[29]. In contrast, other studies found no significant association between HPV positivity and polygamy, female genital mutilation, hormonal contraceptives, multiparity, level of education or number of sexual partners in the last 12 years [28], [30].

4.3 Prevalence of HPV infection among Burkinabe suffering from cervical cancer

Most studies in Burkina have focused on HPV prevalence in the general population in many regions of the country [31]–[34], in HIV-positive individuals [35]–[37], in pregnant women [38], in hepatitis infected women [39], precancerous lesions [26], [40], in cervical cancer [41], and in otorhinolaryngological (ORL) cancers[42]. Very few studies of women diagnosed with cervical cancer have been carried out in Burkina. One involved 112 formalin-fixed, paraffin-embedded archival cervical tissue blocks dated from 2009 to 2015 from women aged between 21 and 84 years. After molecular characterization of the 112 samples, 58.04% had a valid result (beta-globin detected). Of the valid results, 47 samples (72.31%) were HPV-positive. Overall, 11 of the 14 genotypes tested were identified in this study [41]. Of the genotypes found, the most common, in descending order, were HPV18 (25.71%), HPV31 (15.71%), HPV39 (12.86%), HPV16 (12.86%) and HPV45 (12.86%), HPV35 (7.14%) and HPV58 (5.71%) [41]. Among HR-HPV-positive samples, 65.96% of isolated infections and 34.04% of multiple infections were detected, with the number of genotypes ranging from 1 to 4 per individual [41]. Another, which concerns 100 samples (including 83 cervical cancer and 17 precancerous lesions) found 75.9% as HPV prevalence among women with cervical cancer[25]. A third study (review article) [43]synthetizes results of these two studies. The distribution of HR-HPV depending on the histological type of cervical cancer in this study is presented in **table 1**.These prevalencesof HPV in cervical cancer (72.31% and 75.9%) are lower than those found in Ghana (85.4%)[44] and Ivory Coast (89.4%) [45] and far from the 99.7% of HPV positives found in cervical cancer worldwide [46]. These geographical differences in HPV prevalencecould be explained by differences in the number of samples or the method used to detect HPV.

Table I:distribution of HR-HPV depending on the histological type of cervical cancer[43]

	High risk HPV genotypes					
Histological type	HPV16	HPV18	HPV31	HPV33	Others*	Total
Squamous cell carcinoma	7 (5.15%)	28 (20.59%)	11 (8.10%)	20 (14.71%)	55 (40.44%)	**121**
Invasive adenocarcinoma	2 (1.47%)	3 (2.21%)	1 (0.74%)	4 (2.94%)	5 (3.68%)	**15**
Total	**9**	**31**	**12**	**24**	**60**	**136**

*Others: HPV 35, 39, 45, 51, 52, 56, 58, 59, 66, 68.

5.NATIONAL STRATEGIES FOR THE PREVENTION AND MANAGEMENT OF CERVICAL CANCER IN BURKINA FASO

In Burkina Faso, cervical cancer is one of the major public health challenges. In response to this threat, the Burkina Faso government has put in place policies for the prevention, screening and treatment of cervical cancer. Cervical cancer screening plays an important

role in controlling this disease and reducing the number of deaths linked to it. To this end, the ministry of health has set up awareness-raising and free screening campaigns aimed at informing the population of the risks and measures to take to prevent cervical cancer. In addition, the government applies a policy of free care for women and children, which, since 2016, incorporates a free examination to detect the most common cancers including cervical and breast, and free treatment for precancerous cervical lesions [6]. In 2020, the World Health Organization (WHO) adopted a strategy to eliminate cervical cancer, based on three pillars:

- Vaccinate 90% of girls against HPV before the age of 15;

- Screen 70% of women with an effective test between the ages of 35 and 45;

- Treat 90% of women with precancerous lesions and 90% of women with invasive cancer[47]. In order to achieve the first objective, which is to vaccinate 90% of young girls, Burkina Faso, through the ministry of health, has introduced Gardasil 4 (a quadrivalent vaccine that protects against HPV 6, 11, 16 and 18) into the expanded vaccination program for girls aged 9 to 14 since April 26, 2022. Prior to this, a pilot project had been conducted between 2015 and 2017 in two health districts of the country (Baskuy and Solenzo) and 8487 9-year-old girls had been vaccinated [48]. In addition, in 2021, a radiotherapy center was opened at the Centre HospitalierUniversitaire (CHU) de Bogodogo in Ouagadougou to provide better care for cancer patients. Although this center was temporarily closed, the government again launched its reopening in March 2023 [49]. In addition to public sector efforts to improve cervical cancer screening and treatment, private initiatives and community health programs are also being implemented to support the government in the fight against cervical cancer. These include JHPIEGO (Johns Hopkins Program for International Education in Gynecology and Obstetrics) [50]. JHPIEGO is a non-profit Non-Governmental Organization (NGO) that works in several fields, notably in maternal and child health, including cervical cancer screening and treatment. Also, several Burkinabes associations such as KIMI, Espoir Cancer Féminin, ZONTA Club, etc, organize cervical cancer awareness and screening campaigns [4].

6.CERVICAL CANCER SCREENING AND TREATMENT IN BURKINA FASO

Cervical cancer screening in Burkina Faso is based mainly on visual inspection with acetic acid (VIA)with immediate management of precancerous lesions in CHU's, regional hospitals, medical centers and district hospitals since 2012 [51].This method is an alternative to the Papanicolaou test (PAP test) which is not technically and financially feasible in Burkina Faso[52]. It is also the most recommended test in resource-limited settings [53].Cervical cancer screening is also based on the cytological study of smears or biopsies of lesions and/or the HPV test, which uses a molecular biology technique to detect the presence of the virus in cervical cells.However, HPV test is not as commonly used as VIA test because of its cost (around 30 US dollars) [54]. It is mainly used in research and pilot projects like PARACAO (Partnership for Action and Research against Cervical Cancer in West Africa) [55], SUCCESS (Scale Up Cervical Cancer Elimination with Secondary Prevention Strategy project) [56], HARP (The HPV in Africa Research Partnership) [57] studies... Cervical cancer screening rates in Burkina Faso are currently low. A cross-sectional secondary analysis (data from all 13 regions in Burkina Faso) revealed that only 6.2% of women are being screened. The highest rates were observed in the "Hautsbassins"(19.2%) and "Centre" regions (14.7%) while the "Plateau central"(0%) and "Est" regionshad the lowest rates (0 and 0.6% respectively). The screening frequency was 18.5% for urban areasand 2.8% for rural areas[58].In 2020, it was estimated that only 6% of women in Western/Central Africa had

been screened for cervical cancer in their lifetime. Burkina Faso's screening coverage (4%) was higher than Benin (1%), Cote d'Ivoire (2%), and Ghana (3%), but lower than Senegal (8%). To achieve the target of screening 70% of women aged 35-45 years, Burkina Faso needs to screen at least 926,691 women [53]. The most common barriers to screening in Burkina Faso arepoor knowledge[59],mainly lack of awareness about the disease, its screening, not knowing where to get screening, fear of being diagnosed with the disease, distance from the hospital, and financial difficulties[52], particularly for rural women.

Managing of positive screening results passed by cryotherapy, thermocoagulation or Diathermic Loop Resection (DLR) for precancerous lesions.There are also other types of treatment for cancer in general: surgery, which is a loop electrosurgical excision procedure (depending on the progress of the cancer, hysterectomy extended to the peripheral tissues of the uterus), chemotherapy (drug treatment) and radiotherapy (radiation treatment). These treatments are not accessible to all due to their high cost [6].Cervical cancer treatment is very complex and expensive in Burkina Faso. For example, chemotherapy price ranges from 172 to 689 US$ (depending on drugs and protocol used) every three weeks, carried out 6 times, with the possibility of further treatment. However, most people monthly salary is less than 85 US dollars[6]. Consequences are treatment refusals or treatment breaks. Radiotherapy is available in Burkina Faso butis centralized. Moreover, as in most countries in Sub Saharan Africa, most women are diagnosed in advanced stage, and the only suitable treatment options are palliative treatments. These factors are barriers to effectivetreatmentof cervical cancer in Burkina Faso.

7.RESEARCH OF TREATMENTS USING MEDICINAL PLANTS IN BURKINA FASO

Many efforts are being made through research by scientists in Burkina Faso to enable the contribution of traditional medicine using medicinal plants in the fight against cancer in general and cervical cancer in particular [6]. Indeed, some plants have shown real anti-cervical cancer potential. Extracts of *Nelsoniacanescens* showed quite interesting results on Hela and SiHa cervical cancer cell lines, with the best activity observed for methanolic extracts whose half maximal inhibitory concentration (IC_{50}) were 21.72 ± 0.08 µg/ml and 25.30 ± 0.44 µg/ml respectively for the two cell types. In addition, these extracts showed high selectivity on HeLa and SiHa cancerous cells compared to normal L929 cells with a selectivity index of 7.93 ± 0.03 for methanolic extracts for HeLa cells and 7.48 ± 0.05 for ethyl acetate extracts for SiHa cells [60].

Similarly, another study showed that *Hyptissuaveolens* essential oil exerts a dose-dependent antiproliferative activity and acts on the cell cycle of HeLa cells by inducing G0/G1 cell cycle arrest and a decrease in the G2/M phase. However, cytometric analysis did not detect any changes in the subG1 population (linked to apoptosis) in the cancer cells examined and treated with essential oil. However, a significant peak close to the G0/G1 zone most likely related to necrotic cells on HeLa cells was observed [61]. The essential oils of *Cymbopogonnardus*, *Cymbopogonschoenanthus*, and *Lantana camara* also showed antiproliferative activities on cervical cancer HeLa cell lines with IC_{50}s of 142 ± 6.0; 46.17 ± 11.83; 229.27 ± 11.25 µg/ml respectively for each essential oil [62]–[64]. Traditional recipes based on blends of several medicinal plants are also used in cervical cancer treatment research. We have, for example, the *Acti-plus*(IC_{50}=362±27 µg/ml)[65], *Cancerol S*(EC_{50}= 84.6± 5.2 µg/ml)[66],*paanfotiben1*(IC_{50}=112.02±0.03), and *paanfotiben 2*(IC_{50}>1000 µg/ml)[67], recipes which have cytotoxic effect on HeLa cell lines. Figures 1 and 2 summarise effect of medicinal plants and traditional recipes on cervical cancer cell lines.The search for treatments also involves finding plants with antioxidant potential (cancer being linked to oxidative stress) and rich in anti-cancer substances. Thus, two plants,

Diospyrosmespiliformis and *Danielliaoliveri*, used in traditional medicine for the treatment of tumors in two (2) towns in Burkina (Bobo Dioulasso and FadaN'Gourma) showed antioxidant potential by ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)), FRAP (Ferric ion reducing antioxidant power) and DPPH (2,2-diphényl-1-picrylhydrazyl) methods and contained anticancer substances such as flavonoids and total phenolics[68].

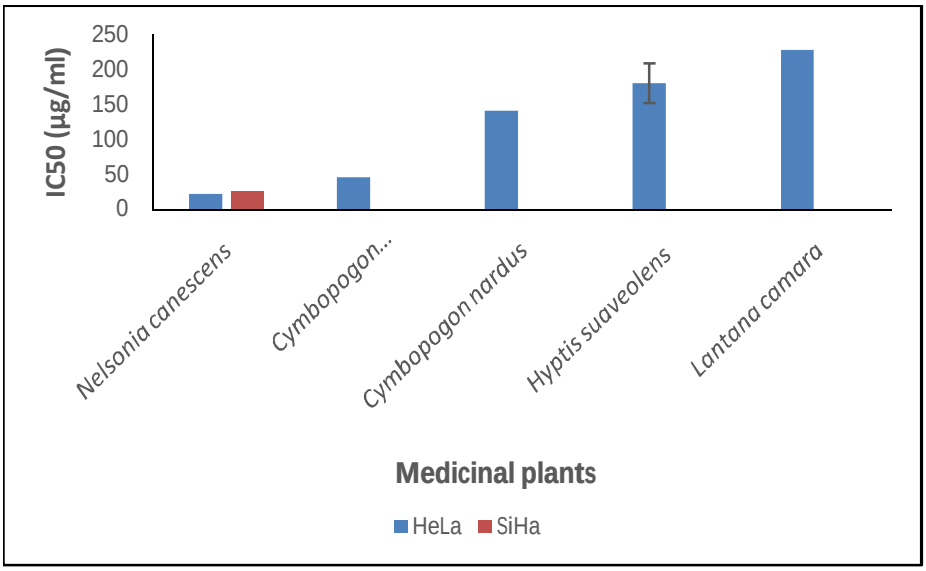

Figure 1: Effect of medicinal plants on cervical cancer cell lines HeLa and SiHa

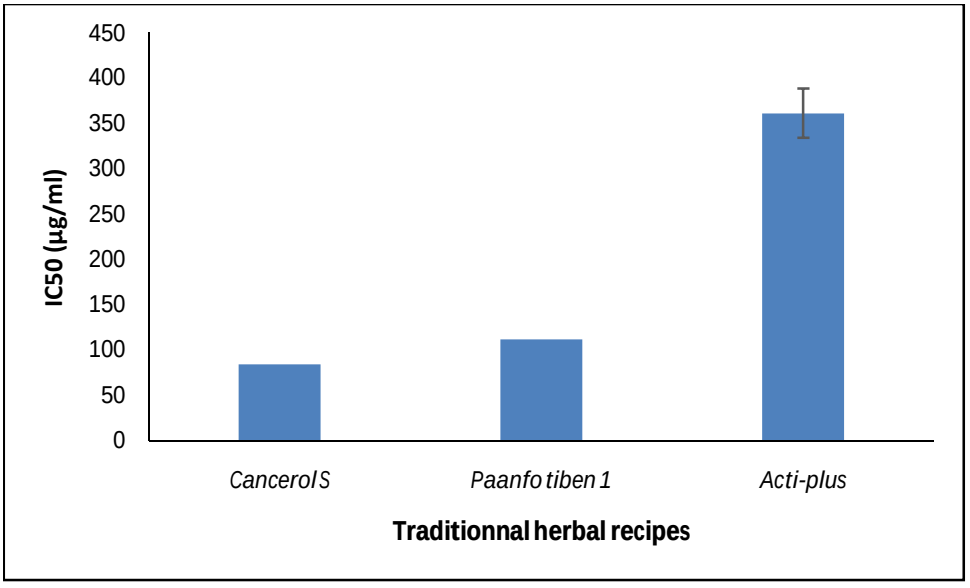

Figure 2: Effect of traditional recipes on cervical cancer cell lines HeLa

8.CONCLUSION

HPV-induced cervical cancer is a so-called preventable cancer. Indeed, HPV vaccination, early detection and treatment of cervical cancer are crucial to prevent the development and progression of the disease. To this end, Burkina Faso, through its Ministry of Health and in collaboration with non-governmental organizations, has set up awareness-raising strategies, free vaccination for girls'aged 9, regular screening campaigns and a radiotherapy center for cancer treatment. However, much remains to be done to combat this disease in this country, especially in terms of public acceptance of the vaccine. It is therefore essential to continue raising women's awareness of cervical cancer. In addition, the search for substances from local medicinal plants used in Burkina Faso to treat tumors could also be an alternative treatment for cervical cancer in this context of limited financial resources and lack of access to anti-cancer molecules.

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