

Review

Gynecological Malignancies in Albania: The Challenges of Cancer Care in a Low Resource Country

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Abstract

Objective: This literature review aims to provide a comprehensive assessment of the current state of gynecological cancers in Albania, including their epidemiology, screening, diagnosis, and treatment. It also aims to highlight the challenges that Albanian patients face in accessing appropriate treatment and to discuss the importance of data collection. This is the first comprehensive review of gynecological cancers in Albania. **Mechanism:** A comprehensive literature search was conducted using various databases to identify relevant studies and government reports. Government reports were used to supplement the data obtained from the International Agency for Research on Cancer and provide additional insights into the challenges and limitations of cancer data collection in Albania. **Findings in Brief:** Albania has a population of 1.18 million women aged 15 years and older who are at risk of developing gynecological cancers. The most prevalent gynecological cancers among Albanian women are endometrial, cervical, and ovarian cancers. Cervical cancer accounts for 30% of all gynecological cancers and is the main cause of cancer-related mortality in this group. Albanian women are at a lower risk of developing gynecological cancers than women in neighboring countries. The main risk factors for gynecological cancers in Albanian women include increasing age, obesity, and human papillomavirus (HPV) infection. However, no data are available on germline mutations associated with a hereditary risk of developing gynecological cancers. Recently, Albania has introduced a cervical cancer screening program along with HPV vaccination. Nonetheless, owing to lack of awareness and education about the disease and limited access to early screening programs, gynecological cancers are often detected at later stages. Treatment options for gynecological cancers in Albania remain largely unchanged and have not adapted to new molecular classification methods that could affect treatment decisions. Furthermore, new therapeutic options, such as immunotherapy and targeted agents, are not commonly used for gynecological cancers in Albania. **Conclusions:** Gynecological cancers remain a significant public health issue in Albania. Urgent action is needed to address the increasing burden of gynecological cancers, including investment in cancer control strategies, primary prevention, early detection, treatment, healthcare infrastructure, capacity building, and research to address specific national needs and implement evidence-based policies.

Keywords: gynecological cancers; ovarian cancer; endometrial cancer; cervical cancer; Albania

1. Introduction

Gynecological cancers, including cancers of the cervix, ovaries, uterus, and vulva, account for more than 6.7% of all cancer-related deaths among women worldwide. The estimated annual incidence of gynecological cancers is more than 1.3 million, with a mortality rate surpassing 671,000 [1]. Despite advances in screening, diagnosis, and treatment, many women still face significant challenges in accessing appropriate care owing to various reasons, including limited access to healthcare facilities and specialized services, lack of knowledge about the disease and its risk factors, and lack of awareness about the importance of early detection [2]. Albania has a population of 1.18 mil-

lion women aged 15 years and older who are at risk of developing gynecological cancers [3]. Despite the scarcity of epidemiological data on gynecological cancers in Albania, it is apparent that early detection through systematic screening and precise diagnosis is paramount for improving outcomes and mitigating the impact of these diseases on women’s health and well-being [4]. In recent years, several screening programs have been introduced in Albania to address the high incidence of gynecological cancers among women [5,6]. These programs aim to increase public awareness about the importance of screening and improve access to diagnostic services. However, despite the availability of screening programs, many Albanian women



still face significant barriers in accessing screening and diagnostic services [5]. The diagnosis and treatment of gynecological cancers present significant challenges for patients in Albania, and access to appropriate care is often limited. These challenges frequently result in delayed diagnosis, ultimately diminishing the efficacy of available treatment options [7]. In this paper, we review the current state of the most frequent gynecological cancers in Albania, including epidemiology, screening, diagnosis, and treatment, and discuss the importance of data collection and access to care and treatment and the challenges faced by Albanian patients. To the best of our knowledge, this is the first comprehensive review of gynecological cancers in Albania.

2. Materials and Methods

A comprehensive literature review was conducted to analyze the current state of cancer data in Albania. This included a review of the comprehensive global cancer statistics published by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) and a review of relevant government reports. In addition, small studies and all published data on cancer in Albania were reviewed to provide a comprehensive picture of the situation. Due to the lack of a national cancer registry in Albania, country-specific rates were estimated based on data from neighboring countries. Government reports were reviewed to supplement the data obtained from the IARC and to provide additional insights into the challenges and limitations of cancer data collection in Albania.

3. Uterine Cancer

Uterine cancer is the 6th most frequent cancer in women and the 15th most common cancer overall with more than 417,000 new cases reported in 2020 worldwide [1]. According to the IARC, the incidence rate of uterine cancer is increasing rapidly and is projected to increase by over 50% worldwide by 2040 [8]. The incidence of uterine cancer has been increasing, particularly in developing countries, owing to lifestyle changes that result in higher rates of obesity and an aging population with longer life expectancies [2]. In 2020, an estimated 197 new cases of uterine cancer and 44 deaths occurred among Albanian women, making it the most common gynecological malignancy. However, compared to neighboring countries, Albanian women have a lower risk of developing endometrial cancer (Table 1, Fig. 1) [9,10].

Uterine cancer is associated with various known risk factors such as increasing age, obesity, smoking, diabetes mellitus, estrogen therapy, chronic anovulation, nulliparity, early menarche, late menopause, family history, and some hereditary syndromes [11–15]. Albania has undergone extensive socioeconomic changes since the fall of its Communist government in 1990, resulting in modifications to its epidemiological profile and health characteristics [16]. For instance, the median age of women in Albania has increased

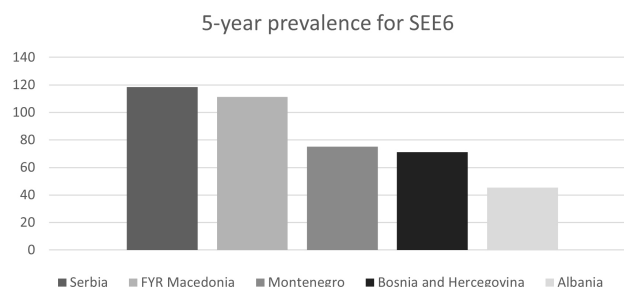


Fig. 1. 5-year prevalence for uterine cancer in South East Europe (SEE6) countries according to Global Cancer Observatory 2020.

by 4.6 years in the past decade, leading to a rapid rise in the average age of the population [17]. Overweight and obesity are also serious public health concerns in Albania, with 45% of women aged 15–49 years being overweight or obese, with a mean body mass index (BMI) of 25.4 kg/m² for women aged 15–49 years and 29.8 kg/m² for women aged 50–59 years [18,19]. The proportion of overweight or obese women increases considerably with age from 14% among women aged 15–19 years to 75% among women aged 40–49 years [18]. Data from case-control studies show that the average age at menarche is approximately 14.4 years, and the mean age at natural menopause is 49 years, which is lower than the average age in Europe [20,21]. According to the WHO, 6% of Albanian women smoked in 2019, and this trend may be continuing to grow [22]. To the best of our knowledge, there is currently no information available on family history or hereditary syndromes associated with uterine cancer in Albania [23].

It has been reported that many types of cancer, including endometrial cancer, are often detected in their later stages in Albania. This is primarily due to a lack of awareness and education about the disease as well as limited access to screening programs [7,24]. Cultural and social factors, such as reluctance to seek medical attention or discuss symptoms with healthcare providers, may also play a role [25]. Additionally, under-funding and a shortage of healthcare resources in Albania can result in delayed diagnosis and treatment [26,27].

In recent years, the management of endometrial cancer has become increasingly complex owing to new molecular classifications that impact surgical management, systemic treatment, and prognosis. Additionally, new immunotherapies and medications targeting specific genetic mutations have been approved [28–33]. However, these new classifications are yet to be implemented in Albania because of limited access to genetic testing and a shortage of trained professionals, such as geneticists or molecular pathologists, who can interpret the results and apply the new classifications. Currently, in Albania, the treatment options for endometrial cancer include surgery, radiation therapy, and chemotherapy [7]. The main surgical method

Table 1. Global Cancer Observatory 2020, Uterine Cancer in South East European (SEE6) countries. Last accessed: 20 December 2022.

Country	No new cases	%	Rank	Cumulative risk	No of deaths	%	Rank	Cumulative risk
Albania	197	2.8	11	1.01	44	1.1	18	0.19
Bosnia and Hercegovina	369	2.5	11	1.38	99	1.1	19	0.32
Republic of North Macedonia	369	4.8	6	2.6	80	1.9	13	0.51
Montenegro	70	2.2	14	1.63	38	2.2	15	0.93
Serbia	1539	3.1	8	2.24	383	1.4	19	0.44

Table 2. Global Cancer Observatory 2020, Cervical Cancer in South East European (SEE6) countries. Last accessed: 20 December 2022.

Country	No new cases	%	Rank	Cum risk	No of deaths	%	Rank	Cum risk
Albania	133	1.9	15	0.71	74	1.9	14	0.38
Bosnia and Hercegovina	312	2.1	15	1.31	153	1.7	15	0.56
FYR Macedonia	113	1.5	15	0.77	62	1.5	16	0.41
Montenegro	113	3.5	7	2.65	54	3.1	10	1.08
Serbia	1205	2.5	10	1.86	634	2.3	12	0.88

for endometrial cancer is hysterectomy; depending on the stage of the cancer, lymph node dissection may also be performed. This is typically performed as open surgery; however, in some cases, it is performed laparoscopically [34]. Access to radiation therapy for cancer treatment is currently limited to only two centers in Albania, making it one of the South East European (SEE) countries with the lowest density of available operating radiation therapy machines (LINACs, brachytherapy, and cobalt-60) [27]. The most commonly used chemotherapeutic drugs for endometrial cancer include doxorubicin, cisplatin, and paclitaxel. Endocrine therapy is usually used in combination with surgery as an adjuvant or palliative treatment in advanced or recurrent cases. Access to immunotherapies and targeted treatments is limited to private healthcare facilities, whereas public healthcare facilities do not have access to these drugs mostly because of their high cost [7,35,36].

4. Cervical Cancer

Cervical cancer is a significant health concern in Albania, with 133 women diagnosed with the disease and 74 deaths annually [10]. It is the fifth most common cancer among women in the country and the second most common cancer among women aged 15–44 years [10]. In comparison to other SEE6 countries, the rate of cervical cancer in Albania is lower but still higher than that in Eastern Mediterranean countries (Table 2) [37].

In Southern Europe, it is estimated that approximately 3.8% of women in the general population have cervical human papillomavirus (HPV)-16/18 infection at any given time. In addition, 68% of invasive cervical cancers in this region are caused by HPV types 16 or 18 [38]. Two studies have been conducted in Albanian women to assess the prevalence of HPV infection. One study conducted in 382 sexually active women aged 18–24 years reported an HPV

infection prevalence of 24.87% with HPV 16 being the most frequent oncogenic type [39]. The other study done in 357 women aged 19–67 years reported an HPV infection prevalence of 45.09% with HPV 16 as the most frequent type (21.74%), followed by HPV 6 (13.66%) and HPV 18 (9.32%) [40]. Until 2018, cervical cancer screening in Albania was mostly based on opportunistic Pap smear tests, which means that tests were performed only when a woman visited a healthcare provider for another reason rather than as part of a systematic screening program [7]. In 2019, a national screening program for cervical cancer using HPV testing was implemented for women aged 40–50 years [5]. The initial report from the program showed an overall prevalence of high-risk HPV of 6.2% [6]. In 2022, a nationwide vaccination program was initiated for 13-year-old girls, using a quadrivalent HPV vaccine and a single-dose schedule [41]. The UK introduced a systematic cervical screening program in 1988 that led to a significant reduction in mortality and increased coverage. The program screens women aged 25–64 years every 3–5 years, and the age range is adjusted to target the most effective group [42,43]. The UK's experience emphasizes the importance of early detection through systematic screening programs to prevent and reduce the burden of cervical cancer.

The majority of cervical cancer cases in Albania are diagnosed in the later stages of the disease when treatment options are limited and the prognosis is poor [7]. Careful monitoring of the screening program is necessary to ensure that it effectively reaches the targeted population and detects precancerous cervical lesions and cervical cancer in the early stages.

The treatment options for cervical cancer in Albania include surgery and radiation therapy, either as a single treatment or in combination. Preneoplastic cases are treated by conization, whereas radical hysterectomy is the

Table 3. Global Cancer Observatory 2020, Ovarian cancer in South East European (SEE6) countries. Last accessed: 20 December 2022.

Country	No new cases	%	Rank	Cum risk	No of deaths	%	Rank	Cum risk
Albania	76	1.1	19	0.42	48	1.2	17	0.26
Bosnia and Hercegovina	317	2.2	13	1.19	205	2.2	11	0.69
FYR Macedonia	111	1.5	16	0.73	67	1.6	15	0.42
Montenegro	56	1.8	16	1.16	39	2.2	14	0.81
Serbia	967	2.0	16	1.41	626	2.2	13	0.81

most common treatment for early stage cervical cancers. In young patients with early invasive cancer, fertility-sparing trachelectomy may be proposed in selected cases, along with a surgical study of nodal status. For advanced stage cervical cancer, the treatment of choice is a combination of radiation therapy and chemotherapy. Concurrent chemotherapy (weekly cisplatin) with radiation therapy is preferred for patients with locally advanced cervical cancer. Between 2009 and 2012, brachytherapy became an available treatment option for patients with cervical cancer [44]. However, following this period, patients requiring brachytherapy had to seek treatment in neighboring countries as this method was no longer available within the country [27]. For patients who are not candidates for surgical resection or salvage radiation therapy, systemic treatment is the first-line option, and regimens typically consist of a platinum-based combination (carboplatin + paclitaxel) and the angiogenesis inhibitor, bevacizumab, as stated in the National Comprehensive Cancer Network (NCCN) guidelines [36,45]. A retrospective study conducted at the Royal Marsden Hospital in the UK between 2004 and 2014 analyzed the outcomes of second-line systemic therapy in 70% of women treated with systemic therapy for recurrent or metastatic cervical cancer. The results showed an objective response rate of 13.2%, a median progression-free survival of 3.2 months, and a median overall survival of 9.3 months [46]. These findings highlight the importance of first-line chemotherapy in the management of recurrent or metastatic cervical cancer and the need for further lines of treatment. This issue is particularly relevant for low-resource countries, such as Albania. Therefore, it is crucial to consider clinical trials whenever feasible, including the use of novel targeted agents and immunotherapy.

5. Ovarian Cancer

Ovarian cancer ranks third among the most common gynecological cancers in Albanian women, with an estimated 76 new cases and 48 deaths occurring annually [10]. Although the rate of ovarian cancer (OC) in Albania is considered low compared to that in other European countries, there may be discrepancies in data sources [47]. According to the Global Cancer Observatory, the incidence of OC in Albania is lower than that in other South East European countries (Table 3) [37].

A retrospective analysis conducted at the Mother Teresa University Hospital Center identified 328 new cases of OC diagnosed between 2012 and 2016, with the median age of patients being 56 years [48]. Risk factors associated with OC include aging, early onset of menstruation, late onset of menopause, nulliparity, and genetic factors [49–51]. Although Albania has a relatively low incidence of OC compared with other countries, its aging population suggests that the number of cases is likely to increase in the future. A case–control study that evaluated the relationship between reproductive factors and OC development reported nulliparity, early age at menarche, and late age at menopause as risk factors in Albanian women [20]. However, to the best of our knowledge, there is currently no available information regarding family history or hereditary syndromes associated with OC in Albania [23]. A study aimed at investigating the frequency of a specific *BRCA1* mutation, c.3700_3704del, in Albanian breast and OC patients from North Macedonia and Kosovo reported the frequency of the mutation as 3.6% in Albanian women from North Macedonia and 7.9% in Albanian women from Kosovo, which is the highest reported frequency worldwide [52]. These findings require further investigation in Albanian women living in Albania to determine whether similar patterns of mutations are present in this population.

Similar to other countries, ovarian cancer is frequently diagnosed at an advanced stage in Albania. This is due to several factors, including the lack of apparent symptoms of the disease, limited awareness, limited healthcare access, and a shortage of diagnostic tools and early detection programs [7,53]. According to data collected at the Mother Teresa University Hospital Center, 67.5% of patients were diagnosed with ovarian cancer at a late stage, while 32.5% of patients were diagnosed at an early stage [48]. The absence of effective screening programs for OC poses a significant financial burden. While precise data on the cost of ovarian cancer treatment in Albania are scarce, in the United States the average initial cost in the first year can reach approximately USD 80,000, with the final year's cost increasing to USD 100,000 [54]. In the past decade, researchers have focused on developing cost-effective strategies for early detection and prevention of OC. However, the development of an effective OC screening strategy presents several challenges. OC is a low-prevalence disease in average-risk women and requires a testing strategy with

high specificity and sensitivity to minimize false-positive results. Therefore, OC screening is not recommended for average-risk women [55,56]. Identifying women at high risk for hereditary cancer syndrome through a family history is essential. Such women would benefit from genetic testing, genetic counseling, and referral for risk reduction strategies, such as risk-reducing bilateral salpingo-oophorectomy, if they have a hereditary cancer syndrome (e.g., *BRCA1*, *BRCA2*, and Lynch syndrome) [57].

Ovarian cancers are staged surgically and pathologically. Total hysterectomy and bilateral salpingo-oophorectomy with pelvic and para-aortic lymph node dissection is the standard staging procedure [48]. Debulking surgery is performed when metastases are evident. Systemic treatments for OC commonly involve chemotherapeutic drugs such as carboplatin, paclitaxel, gemcitabine, and doxorubicin as well as the monoclonal antibody bevacizumab [36,48]. Genetic testing is playing an increasingly important role in the management of OC with a rapid introduction of poly (ADP-ribose) polymerase inhibitors (PARPi) into the treatment paradigm. In the last decade, molecular characterization of OC has revealed that over 50% of high-grade serous OCs (HGSOCs), which account for 80% of epithelial OCs (EOCs), have a defect in homologous recombination repair, explaining their extreme sensitivity to platinum drugs; this defect is characterized by genetic and epigenetic alterations in genes involved in the pathway, including *BRCA 1* and *2*, as demonstrated by many studies, including the Cancer Genomic Atlas [58,59]. This underlying defect not only supports the sensitivity to platinum agents but also allows the clinical implementation of targeted therapy with (PARPi), such as olaparib, rucaparib, and niraparib, which have been approved by the European Medicines Agency (EMA) and Food and Drug Administration (FDA) for the treatment of OC [60]. Although PARPi have been shown to be clinically effective in treating OC, they have not yet been registered or reimbursed in Albania [36]. Additionally, there is limited utilization of molecular testing to inform treatment decisions to patients with OC in Albania, which may further affect the quality of care provided [7].

6. Discussion

In this review, we present an overview of gynecological cancers in Albania. The results revealed that these cancers are a significant public health issue in the country, with uterine, cervical, and ovarian cancers being the most common types [1,10]. Addressing the rising incidence and mortality rates of gynecological cancers and late-stage diagnosis in Albania requires a combination of strategies, including promoting healthy lifestyles, increasing access to healthcare services, improving the availability of diagnostic tools and screening programs, and improving the training and capacity of healthcare professionals.

New molecular classifications, combined with new drug classes, have revolutionized precision medicine for patients with endometrial cancer. International guideline committees, including the NCCN and European Society for Medical Oncology, provide recommendations on the molecular classification of endometrial carcinoma [61]. Albania faces challenges in implementing these guidelines owing to various constraints such as a shortage of qualified professionals, limited availability of molecular testing, and inadequate coverage for systemic treatments such as targeted therapy or immunotherapy in public healthcare facilities.

Cervical cancer accounts for 30% of all gynecological cancers and is the main cause of cancer-related mortality in this group [10]. While Albania has made strides in implementing a national HPV screening program, there is room for improvement in terms of increasing coverage and promoting awareness. Additionally, monitoring and evaluating the effectiveness of the screening program and making adjustments as needed can help ensure that it reaches its full potential in preventing cervical cancer.

The high fatality rate of OC in Albania underscores the need for personalized prevention strategies and improvements in diagnosis and treatment. *BRCA1/2* mutations are the strongest known genetic risk factors for epithelial OC and are found in 6–15% of women with EOC. Therefore, identifying these mutations in OC patients can provide important information regarding treatment options. Genetic counseling and testing for inherited mutations associated with OC are essential tools that can provide important information for prevention and early diagnosis. However, lack of coverage for genetic mutation tests in Albania limits the availability of these tests, leading to suboptimal treatment options and outcomes [23]. The treatment paradigm for EOCs, particularly for HGSOC, has undergone significant changes in recent years following the introduction of PARPi. Therefore, identifying women with *BRCA1/2* mutations and homologous recombination-deficient EOCs has significant clinical implications for chemotherapy regimen planning and the use of targeted therapies such as PARPi [62].

Establishing a comprehensive national cancer registry is crucial for collecting data on the incidence, mortality, and survival rates of various types of cancers, as well as the types of treatments received by patients. Such a registry would help identify the specific needs of Albania and enable evidence-based policies to address the increasing burden of gynecological cancers.

7. Limitations

Limitations of this literature review are primarily related to the lack of a national cancer registry in Albania. The country-specific rates were estimated based on data from neighboring countries, which may not accurately reflect the true situation in Albania. Furthermore, the lack of a central-

ized cancer registry may have led to underreporting of cancer cases and incomplete data, which could have affected the overall analysis of the cancer burden in Albania. In addition, the small number of studies and published data on cancer in Albania may have limited the scope and comprehensiveness of this review. Despite these limitations, this literature review provides valuable insights into the current state of cancer data in Albania and highlights the need for further investment in cancer research and infrastructure to address the challenges faced by the country in managing gynecological cancers.

8. Conclusions

In conclusion, this review emphasizes the urgent need for investment in cancer control strategies, primary prevention, early detection, treatment, healthcare infrastructure, capacity building, and research to address specific national needs and implement evidence-based policies.

Author Contributions

KM, CP, OP and CR conceived and designed the review; KM, EC, KQ, JP, AE, FS collected the data and references; KM and CP wrote the paper; CP, OP, EC, KQ, JP, AE, FS and CR revised the manuscript. All authors read and approved the final manuscript. KM and CP contributed equally.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. Cesare Romagnolo is serving as one of Guest editors of this journal. We declare that Cesare Romagnolo had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Michael H. Dahan.

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