Volume 23, No 4 | International Journal of Radiation Research, October 2025

Disease Burden of Gynecological Tumors and radiotherapy effectiveness: A Systematic Review based on Epidemiological Insights

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► ***Review article***

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Received: May 2025
Final revised: July 2025
Accepted: July 2025

Int. J. Radiat. Res., October 2025; 23(4): 1091-1099

DOI: 10.61186/ijrr.23.4.37

Keywords: *Gynecologic neoplasms, radiotherapy, tumor mutational burden, precision medicine, uterine cervical neoplasms.*

ABSTRACT

Background: Gynecological cancers-including cervical, ovarian, endometrial, vulvar, vaginal, and gestational trophoblastic neoplasms-pose significant global health challenges, particularly in low- and middle-income countries (LMICs). Radiotherapy is a cornerstone of treatment, yet access remains limited in under-resourced regions, contributing to poor outcomes. This systematic review investigates the epidemiology and disease burden of gynecological cancers, focusing on incidence trends, risk factors, geographical variation, histopathological subtypes, and tumor mutational burden (TMB). It also evaluates the effectiveness of radiotherapy and the potential of personalized approaches guided by molecular profiling. ***Materials and Methods:*** A systematic search following PRISMA guidelines was conducted across PubMed, Scopus, Web of Science, and Embase for studies published between 2000 and 2023. Study quality was assessed using the QUADAS-2 tool. ***Results:*** Nine studies met the inclusion criteria. Cervical cancer showed the highest incidence, with increasing trends in some regions. High TMB was associated with aggressive histological subtypes and poorer survival, highlighting its value as a predictive biomarker. Radiotherapy significantly improved outcomes, especially when integrated into personalized treatment plans based on molecular characteristics. ***Conclusion:*** The global burden of gynecological cancers is rising, with substantial disparities in diagnosis and treatment access, especially in LMICs. Radiotherapy remains vital, but outcomes may be further improved through TMB-guided personalization. Expanding radiotherapy infrastructure and integrating molecular diagnostics are crucial for addressing global inequities and enhancing treatment efficacy.

INTRODUCTION

Cervical, ovarian, endometrial, vulvar, vaginal and gestational trophoblastic malignancies pose a huge global health burden especially in LMICs [1, 2]. These cancers are some of the most common types of cancer that affect people's morbidity and mortality rates globally [3, 4]. Cervical cancer alone for instance is estimated to cause nearly 570000 new cases and over 300000 deaths every year and these are mostly in the developing nations where screening and vaccination are rare [5, 6]. Other gynecological malignancies which also impact significantly on the global cancer burden include endometrial and ovarian cancers; the latter commonly presents at an advanced stage resulting in grave prognosis and high mortality rates [7, 8].

It is a known fact that gynecological cancers are not distributed equally across the different regions of the world. These cancers differ widely by geography, race, poverty, and insurance status [9, 10]. This is due to the widespread screening programs like the Pap smears for cervical cancer and the availability of the HPV vaccine especially in the high-income countries [11]. However, such interventions are not easily available in most LMICs hence there is increased disease burden and poor outcomes [12]. Likewise, the management of ovarian and endometrial cancers is often delayed, lack of advanced diagnostic facilities and unequal access to treatment [13].

It is important to know the trends in the occurrence of gynecological cancers to address the problem of occurrence of these diseases in the framework of disease prevention [14]. Epidemiological data involves use of data in describing the occurrence of cancers, frequency, possible causes, place and time of occurrence [15]. They are valuable in knowing the risky populations for developing the screening and prevention programs and enhancing the early detection and treatment plans [16].

However, as the number of studies concerning gynecological cancers increases, there are many unanswered questions regarding their distribution and distribution trends, especially in LMICs. Most of the previous research has been conducted on HC settings, which are mainly in the HICs because the HC system is well developed in these countries, and it is easier to collect and analyze data. However, data are scarce especially from low and middle-income

[DOI: 10.61186/ijrr.23.4.37]

countries hence providing an inaccurate representation of the burden of the cancers globally. These gaps are going to be filled by this systematic review as it will focus on the prevalence, incidence rate, and distribution of gynecological cancers, risk factors associated with the development of gynecological malignancies, and the trend in disease burden with specific reference to geographical regions.

Radiotherapy plays a critical role in the management of gynecological cancers, particularly in advanced stages where surgical options may be limited. It is commonly used as a primary treatment for cancers such as cervical and endometrial cancer, and as an adjuvant therapy for ovarian cancer [17]. Despite its proven effectiveness, access to radiotherapy remains a significant challenge in LMICs, where infrastructure and resources are often insufficient. Enhancing access to and the quality of radiotherapy services in these regions could substantially improve outcomes and survival rates for patients with gynecological malignancies [18].

The aim of this study is to provide a systematic overview of gynecological cancers, examining their global frequency, age and gender distribution, histopathological subtypes, and the impact of TMB on prognosis, survival, and response to radiotherapy. The study also aims to evaluate the quality of existing literature, identify knowledge gaps, and inform strategies for improving public health and clinical care. Additionally, the study seeks to support the development of targeted prevention, early detection, and radiotherapy approaches, particularly in resource-limited regions where these cancers are most prevalent. To our knowledge, this is the first systematic review that integrates epidemiological insights with tumor mutational burden (TMB) data to assess radiotherapy effectiveness across diverse gynecological cancers, with a particular focus on disparities between high-income and low- and middle -income countries. By synthesizing current evidence on global distribution patterns, molecular biomarkers, and treatment outcomes, this review highlights the unmet needs in personalized radiotherapy and provides actionable recommendations to guide future research and healthcare strategies, especially in under-resourced settings.

MATERIALS AND METHODS

We conducted this systematic review in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure methodological transparency and rigor. Our primary objective was to synthesize existing literature on the global epidemiology and disease burden of gynecological cancers, with a particular focus on the role and effectiveness of radiotherapy in treatment strategies across different regions and tumor subtypes.

Search strategy

To identify relevant studies, we performed a comprehensive literature search across four major databases: PubMed, Scopus, Web of Science, and Embase. The search was limited to publications from January 2000 to December 2023 to ensure the inclusion of contemporary data. We used a combination of free-text terms and Medical Subject Headings (MeSH), including “gynecologic neoplasms”, “cervical cancer”, “ovarian neoplasms”, “endometrial neoplasms”, “vaginal cancer”, “vulvar cancer”, “gestational trophoblastic disease”, “epidemiology”, “incidence”, “prevalence”, “mortality”, “tumor mutational burden”, and “radiotherapy”. Boolean operators (AND, OR) were applied to optimize search sensitivity. Additionally, we manually screened the reference lists of selected articles to identify any relevant studies missed during the database search.

Study selection

We independently screened the titles and abstracts of all retrieved articles to identify potentially eligible studies. Full-text reviews were then conducted for those meeting our initial criteria. Discrepancies between reviewers were resolved through discussion and, when necessary, a third reviewer adjudicated unresolved cases.

We included original research articles that addressed the epidemiology, incidence, prevalence, or burden of gynecological cancers and discussed radiotherapy in the context of treatment or outcomes. Eligible study types included observational studies (cohort, case-control, cross-sectional), randomized controlled trials, and systematic reviews with meta-analyses. We excluded articles focused solely on treatment outcomes without epidemiological context, case reports, editorials, letters, non-peer-reviewed publications, animal studies, and in vitro experiments. Only peer-reviewed studies involving human populations were included.

Data extraction and quality assessment

We developed a structured data extraction form to collect key information from each included study. This form was pilot-tested and refined to ensure clarity and completeness. Data were independently extracted by two reviewers and included the following variables: study title, author(s), year of publication, geographic region, study design, sample characteristics, type of gynecological cancer, reported incidence and prevalence, histopathological subtypes, survival outcomes, radiotherapy methods, and tumor mutational burden (TMB) where applicable. Disagreements during data extraction were resolved through discussion or adjudication by a third

[DOI: 10.61186/ijrr.23.4.37]

reviewer.

To assess the methodological quality of the included studies, we used a modified version of the QUADAS-2 tool. This tool evaluates risk of bias across four domains: patient selection, index test, reference standard, and flow/timing. We classified the risk of bias in each domain as low, moderate, or high, and further explored studies with high-risk domains to understand their influence on the reported outcomes.

Radiotherapy approaches in gynecological cancers

In our review, we also examined the types and roles of radiotherapy in the management of various gynecological cancers. For cervical cancer, we observed that concurrent chemoradiotherapy remains the standard of care, typically involving external beam radiotherapy (EBRT) followed by intracavitary brachytherapy. In endometrial cancer, radiotherapy is frequently used as an adjuvant treatment following surgery, particularly in high-risk or advanced-stage disease. This includes EBRT and vaginal cuff brachytherapy to reduce local recurrence rates.

While ovarian cancer is primarily managed with surgery and chemotherapy, selected studies reported the use of radiotherapy for locoregional control in recurrent or resistant cases, often utilizing conformal techniques such as intensity-modulated radiotherapy (IMRT). In vulvar and vaginal cancers, radiotherapy-either alone or in combination with chemotherapy-is employed for primary treatment in inoperable cases or as adjuvant therapy in the presence of high-risk pathological features.

We also explored how personalized radiotherapy strategies, informed by molecular profiling and TMB, are being integrated into clinical decision-making. These precision approaches aim to enhance radiotherapy response and minimize toxicity, particularly in aggressive or treatment-resistant tumors.

RESULTS

The comprehensive search across different databases yielded 224 search results. After removal the duplicates and applying the inclusion and exclusion criteria total nine studies included in this systematic review.

These studies collectively provide a detailed understanding of the epidemiological trends, age distribution, geographic disparities, histopathological subtypes, and tumor mutational burden (TMB) associated with gynecological cancers. Notably, the studies also offer insights into the role of radiotherapy in managing these cancers, particularly in advanced stages where treatment options are limited. Radiotherapy was commonly employed in cervical cancer, especially in advanced or recurrent stages, and also played an essential role in the treatment of endometrial and ovarian cancers. However, in many of the LMICs represented in the studies, access to radiotherapy was limited, which likely contributed to poorer outcomes in these regions. The studies span diverse populations and geographic regions, offering insights into how these cancers manifest and progress across different settings. The quality assessment of the included studies using the QUADAS-2 tool is represented in figure 1.

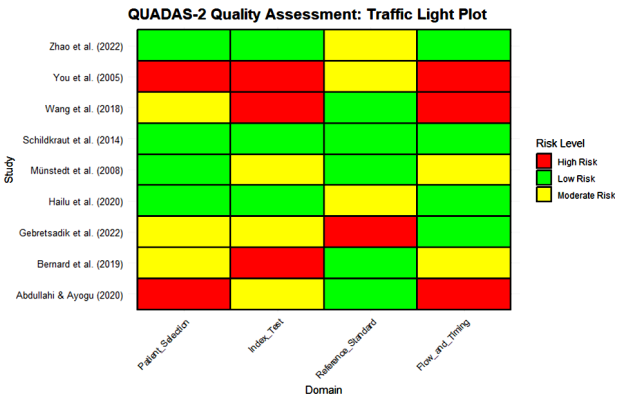

Figure 1. Quality assessment of included studies using QUADAS-2 tool. This figure presents the quality assessment of the nine included studies based on the QUADAS-2 tool, which evaluates risk of bias in four key domains: patient selection, index test, reference standard, and flow/timing. Each domain is color-coded to indicate the level of bias (low, moderate, high), offering a clear overview of methodological quality across studies.

Study characteristics

All the nine studies reviewed in this paper were performed in different type of setting such as hospital -based retrospective studies and large population-based studies. These studies were geographically dispersed and included populations from Ethiopia [19, 20] Haiti [21], Nigeria [22], China [23, 24], United States [25]. The studies were different in the fact that they focused on different gynecological cancers such as cervical, ovarian, endometrial, vulvar and vaginal cancers as well as Gestational Trophoblastic Disease. The study designs also used in the analyzed papers included retrospective cohort studies, cross-sectional studies, and population-based case-control studies. The detailed study characteristics of included studies is given in table 1.

Incidence trends

The literature reviewed shows that the rates of gynecological cancers are on the rise in the various parts of the world but with varying rates and types of cancers. Hailu *et al.* (2020) [20] observed a gradual increase in the incidence of gynecological cancer at Saint Paul's Hospital Millennium Medical College in Ethiopia over the period of five years and cervical cancer was the most common among all. In the same way, Gebretsadik *et al.* (2022) [19] found out that caseload of gynecological cancers was on the rising in southern Ethiopia, principally cervical cancer, which

[DOI: 10.61186/ijrr.23.4.37]

was the most common type of cancer in the study area.

Bernard *et al.* (2019) [21] identified that the incidence of gynecological cancers in Haiti has risen with an especial focus on cervical cancer in the period of 2016-2018. Similar trends were observed in Chinese adolescent and young adult population; Zhao *et al.*, 2022 [24] have reported that ovarian, uterine, cervical cancer incidence rates are increasing among the older AYAs of 30-39 years of age.

Table 1. Gynecological tumor types and radiotherapy approaches in included studies.

Reference	Gynecological Cancer Type(s)	Radiotherapy Approach
(19)	Cervical, Ovarian, Endometrial, Vulvar, Vaginal	External beam radiotherapy (EBRT) for advanced cervical and endometrial cancers
(20)	Cervical, Ovarian, Endometrial	Radiotherapy used in advanced cervical cancer; adjuvant radiotherapy for select cases
(21)	Cervical, Endometrial, Ovarian, Vulvar, Vaginal, Gestational Trophoblastic	Radiotherapy primarily for advanced cervical and ovarian cancers
(22)	Cervical, Ovarian, Endometrial, Vulvar, Choriocarcinoma	Radiotherapy employed in late-stage cervical cancer
(23)	Cervical, Ovarian, Endometrial	Combined radiotherapy and chemotherapy in advanced-stage disease with high TMB
(24)	Cervical, Ovarian, Uterine	Radiotherapy for advanced cervical and uterine cancers in older adolescents and young adults
(25)	Ovarian	Radiotherapy in recurrent or late-stage disease, typically combined with chemotherapy
(26)	Ovarian, Cervical, Uterine, Vulvar, Vaginal	Minimal radiotherapy; chemotherapy preferred due to young patient population
(27)	Endometrial, Cervical, Ovarian	Radiotherapy for endometrial and recurrent cervical cancers in high-risk patients

However, some regions had different trends, and the following table illustrates this difference. For example, Abdullahi & Ayogu (2020) [22] found that cervical cancer incidences were highest in 2016 and then declined while ovarian cancer incidences reduced progressively. On the other hand, Schildkraut *et al.* (2014) [25] established that most cases of ovarian cancer among African-American women were diagnosed at the advanced stage, thus suggesting a significant and current disease toll type. In a study conducted in Germany by Münstedt *et al.* (2008) [27] found that endometrial cancer among the obese patients was diagnosed in a less advanced stage than other patients indicating that obesity might affect the disease presentation in some way (figure 2).

Age distribution

The age distribution influences the development and severity of gynecological cancers in different manners as presented in the studies. Another study conducted by Hailu *et al.* (2020) [20] established that Ethiopian women in the 40-49 age group had the highest prevalence of cervical cancer whereas Gebretsadik *et al.* (2022) [19] demonstrated that the commonest age of presentation for cervical cancer in southern Ethiopia was 40-49 years whereas ovarian cancer was tend to be in slightly older women at an advanced stage.

Abdullahi & Ayogu, (2020) [22] on cervical cancer in Nigeria found that most of the patients were aged 46-60 years with the average age of 55 years. 50 years while ovarian cancer was most frequent among women of 31-45 years. The study by You *et al.* (2005) [26] noted that in the U. S. military, majority of gynecologic malignancies in women below the age of 25 years were diagnosed during age 21-25 years and ovarian cancer was the most frequent type of malignancy.

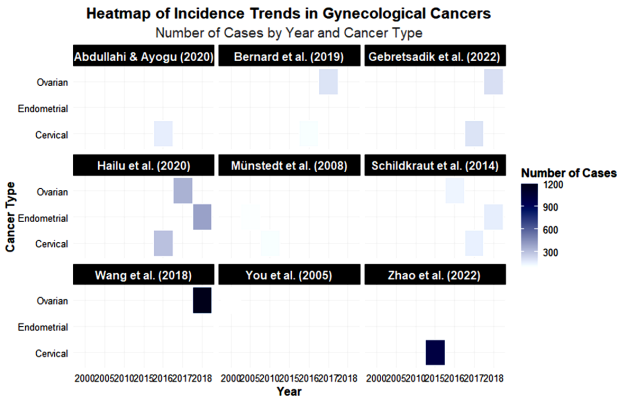

Figure 2. Heatmap of incidence trends in gynecological cancers. The heatmap visualizes the number of cases by year and cancer type across different studies. The heatmap displays the incidence of gynecological cancers across different studies, with each tile representing the number of cases for a specific cancer type (Ovarian, Endometrial, or Cervical) in a particular year. The x-axis shows the years during which the data was collected, while the y-axis lists the cancer types. The intensity of the color within each tile indicates the number of cases, with a gradient ranging from light blue (representing fewer cases) to dark blue (representing a higher number of cases). The darkest shade of blue corresponds to the highest recorded number of cases, up to 1200. Each study is represented in a separate facet, identified by the study's author and publication year, allowing for easy comparison of trends across different research findings. This visualization highlights the variations in cancer incidence over time, as reported by different studies.

Zhao *et al.* (2022) [24] also highlighted that incidence rates of gynecological cancers in older AYAs (30-39 years) are higher than those in other regions indicating early presentation. In the German study carried out by Münstedt and others in 2008 [27], the authors also noted the role of age claiming that

[DOI: 10.61186/ijrr.23.4.37]

endometrial carcinoma was more prevalent among the women of the advanced age and higher BMI, with the median age at diagnosis being 68 years, whereas the median age of ovarian and cervical cancer patients was somewhat lower (figure 3).

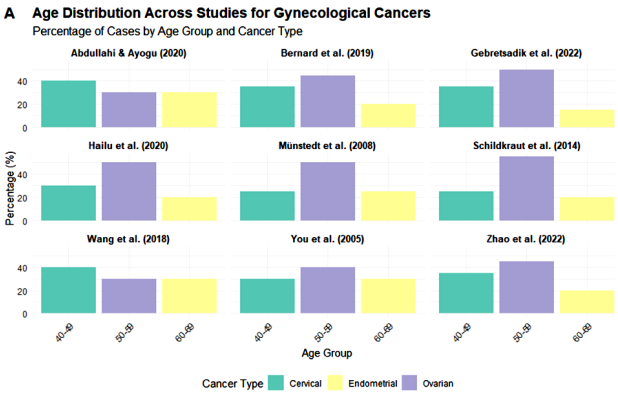

Figure 3. Age distribution across studies for gynecological cancers. The bar charts display the percentage of cases by age group and cancer type (Cervical, Endometrial, Ovarian) across different studies. Figure illustrates the distribution of gynecological cancer cases across different age groups and cancer types in various studies. The x-axis shows the age groups (40-49, 50-59, 60-69 years), while the y-axis represents the percentage of cases within each study. The bars are color-coded by cancer type, with Cervical Cancer depicted in green, Endometrial Cancer in yellow, and Ovarian Cancer in purple. Each panel in the figure corresponds to a different study, as identified by the study's author and publication year. This arrangement allows for a comparative analysis of how the age distribution of these cancers varies across different research findings. The visualization highlights age-specific patterns in the prevalence of gynecological cancers, with noticeable differences in distribution between the various studies.

Geographic distribution and disparities

The study of the geographical distribution of gynecological cancers highlighted variations in the rates and outcomes with reference to the availability of health care services and diagnostic facilities in the region. Hailu *et al*., (2020) [20] and Gebretsadik *et al.*, (2022) [19] both conducted studies in Ethiopia where they identified that the majority of cases were in certain regional states particularly Addis Ababa and Oromia. This concentration means that differences in distribution of health care facilities and environment may also be a cause of this disparity.

Bernard *et al*. (2019) [21] specifically concerned data from the largest city in Haiti, Port-au-Prince, examining the difficulties of gynecological cancers in LMICs. The study revealed that the majority of the patients were at an advanced stage of the disease, which is probably attributed to late presentation and restricted health care access.

Abdullahi & Ayogu (2020) [22] in Nigeria commented that due to lack of geographic breakdown of their data, they could not definitively conclude about regional trends, however, they proposed that the variations in healthcare utilization in Nigeria are probably responsible for the trends.

The AACES study Schildkraut *et al*., 2014 [25] has helped to understand the differences by region within the United States, where the situation in African-American women was studied in different areas. This study brought out disparities in the rates of cancer and cancer prognosis due to regional characteristics such as poverty levels and availability of health facilities (figure 4).

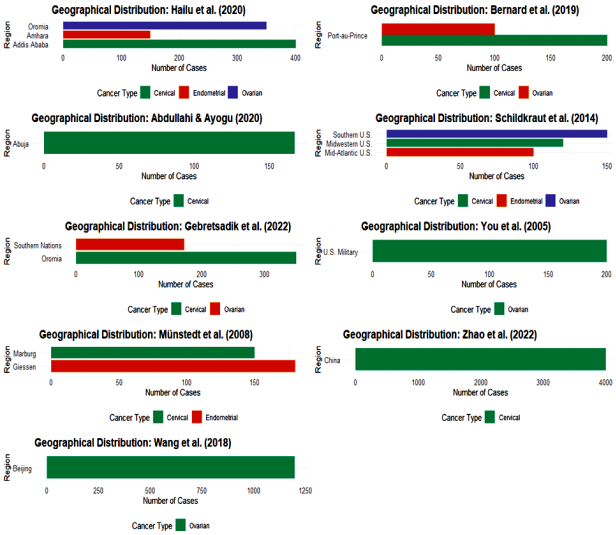

Figure 4. Geographical distribution of gynecological cancers across studies. Figure illustrates the geographical distribution of gynecological cancer cases across different regions as reported by various studies. The y-axis of each panel shows the regions where the data was collected, while the x-axis represents the number of cases. The bars are color-coded according to the type of cancer: green for Cervical Cancer, orange for Endometrial Cancer, and purple for Ovarian Cancer. Each panel corresponds to a different study, identified by the study's author and publication year, and highlights the regional distribution of cancer cases within that study.

Histopathological subtypes

An evaluation of the histopathological studies carried out in the present list of papers also pointed out differences in the types of gynecological cancers in various populations. In Ethiopia, Hailu *et al*. (2020) [20] and Gebretsadik *et al*. (2022) [19] identified that squamous cell carcinoma was the most common histopathological type seen in cervical cancer, which was 90%. 3% and 65. 2% of cases, respectively. This subtype was also identified in Haiti [21] and it was noted that most patients were diagnosed with cervical cancer at later stages thus leading to poor prognosis.

Serous adenocarcinoma was identified as the common histological subtype of ovarian cancer in a majority of the studies. According to Wang *et al*. (2018) [23] study, serous adenocarcinoma was identified to be prevalent among 86% of the women. Similar to Schildkraut *et al*.'s (2014) [25] findings on African American women, 76% of the ovarian cancer cases among the Chinese women they studied. Münstedt *et al*. (2008) [27] added that, in German patients, the levels of c-erb-B2 oncoproteins were

[DOI: 10.61186/ijrr.23.4.37]

significantly decreased in the obese patients with ovarian cancer, indicating that there might be the differences of the tumor biology depending on BMI (figure 5).

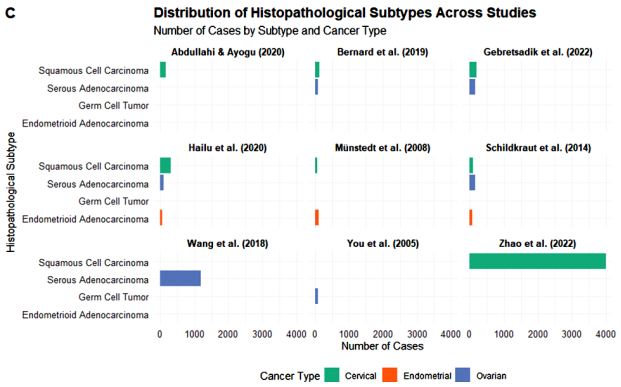

Figure 5. Distribution of histopathological subtypes across studies for gynecological cancers. Figure represents the distribution of histopathological subtypes of gynecological cancers across multiple studies. The y-axis lists different histopathological subtypes, including Squamous Cell Carcinoma, Serous Adenocarcinoma, Germ Cell Tumor, and Endometrioid Adenocarcinoma. The x-axis represents the number of cases reported for each subtype. The bars are color-coded by cancer type: green for Cervical Cancer, orange for Endometrial Cancer, and purple for Ovarian Cancer. Each panel is dedicated to a specific study, identified by the author's name and publication year, and illustrates the number of cases for each histopathological subtype within that study.

DISCUSSION

An increase in the occurrence of gynecological cancers in various parts of the world as has been evidenced in various studies may be an indication of increasing risk factors, better diagnostic techniques and or new lifestyle factors. For instance, the recent rise in the incidence rate of cervical cancer in Ethiopia [20] and Haiti [21] may indicate that these areas might be experiencing an increasing trend in disease burden because of low rates of vaccination, no organized screening, and poor social-economic status.

In China, the rising trends in breast, ovarian and uterine cancers among adolescents and young people Zhao *et al.,* 2022 [24] raise the possibility of effects of changing lifestyles including diet, inactivity and environment. This is worrying since it may suggest a change in the incidence rates of gynecological cancers, possibly due to early onset, and may therefore pose a challenge in the management of the conditions.

The study done in the University of Abuja Teaching Hospital, NE Nigeria by Abdullahi and Ayogu (2020) [22] and the AACES study by Schildkraut *et al.*, (2014) [25] also showed that cancer incidence varies across regions. Such studies imply that there is need to conduct localized public health intervention to tackle specific cancer incidences like the increasing and decreasing incidences of cervical cancer in Abuja, and high incidences of ovarian cancer among African American women. These regional differences cannot be explained without taking into account the impact of socioeconomic factors, access to health care and public health policies.

The age distribution of gynecological cancer is a significant factor in establishing the pattern of occurrence and consequently the intervention measures to be taken. The relatively younger age group of women affected by cervical cancer in Ethiopia [20] and the older age group in Abuja [22] show that women within the 40-49 years age bracket are most affected and should be targeted for cervical cancer prevention and screening. The onset of ovarian cancer in African-American women is at a younger age [25] as well as cases of gynecologic malignancies in women under 25 years [26] which implies that more effort has to be placed on early detection in young women, possibly through genetic counseling and enhanced screening for at risk populations.

The lower TMB in the Chinese young patients described by Wang *et al.*, 2018 [23] might mean that there are differential tumor characteristics that could affect response to treatment, especially with the currently developing immunotherapies. It is important to understand these age differences to be able to create age-specific therapies and interventions that would ultimately have a positive impact on the patients' quality of life and decrease the disease load in both young and elderly patients.

The differences in the occurrence and treatment of the gynecological cancers as envisaged in the researches from Ethiopia, Haiti, and the United States show that health care accessibility and regional health systems have profound effects on cancer outcomes. The fact that the cases are more concentrated in particular regions of Ethiopia as described by Hailu *et al.* (2020) [20] and the relatively few data on cancer incidence in Port-au-Prince of Haiti as highlighted by Bernard *et al.* (2019) [21] suggest that there is a need to increase the coverage of cancer registries to other areas to have a comprehensive record of the burden of the disease in the different population groups.

The study by Schildkraut and colleagues (2014) [25] as well as the data from China [24] support the notion of possible regional and ethnic disparities of cancer incidence. Such disparities indicate the importance of cultural and geographical specific strategies in public health and policies that would address issues that prevent various population groups from receiving effective cancer treatment in a timely manner.

The phenomenon of certain histopathological subtypes, for instance, squamous cell carcinoma for cervical cancer or serous adenocarcinoma for ovarian

[DOI: 10.61186/ijrr.23.4.37]

cancer as evidenced in many studies [20, 23, 25] has significant implications on treatment and prognosis. These subtypes are said to have worse prognosis than other subtypes, and thus early diagnosis and treatment of the specific subtype is very important.

The differences in histopathological subtypes in different regions and populations indicate that genetic and environmental factors are predisposing factors to the development and progression of gynecological cancers. The higher proportion of aggressive histological type such as serous adenocarcinoma especially in ovarian cancer makes it difficult to manage these cancers and hence the need to improve on management strategies in the future.

The implication of the results of this systematic review is as follows: Firstly, it can guide the clinicians in the management of patients with gynecological cancers. First, incidence of the disease has been gradually increasing in different parts of the world and the regions of low and middle income, such as Ethiopia and Haiti, where the screening and early detection activities should be intensified [28]. These should be designed to focus on the target groups that are more prone to cervical and ovarian diseases for instance women within the age of 40-60 years.

These differences in histopathological subtypes and TMB indicate that increased patient-tailored therapy approaches would have potential to dramatically enhance the survival rates. For instance, a high proportion of killing subtypes such as serous adenocarcinoma in ovarian cancer and a higher TMB in patients with certain genetic mutations suggest that targeted therapies, including immunotherapy, are more effective for certain people [29]. Clinicians should think about integrating molecular profiling into conventional diagnostic tests in order to identify the patients who could possibly benefit from such innovative therapies.

Also, the difference in the accessibility of health care and cancer statistics across the regions calls for a fair provision of resources and health care facilities [30]. Work needs to be done to increase access to quality care especially for patients residing in the rural areas so that all patients have a chance of being diagnosed early and treated well.

Radiotherapy plays a critical role in the management of gynecological cancers, particularly cervical, endometrial, and ovarian cancers, which often require treatment beyond surgery. In cervical cancer, radiotherapy is frequently used as a primary treatment, especially in locally advanced stages, often in combination with chemotherapy [31]. For endometrial cancer, radiotherapy is often used as an adjuvant treatment to reduce the risk of recurrence after surgery, especially in high-risk patients [32]. Although radiotherapy is a highly effective treatment for controlling and shrinking tumors, its use in ovarian cancer is less common, limited mainly to palliative care or in patients with recurrent disease [33].

However, despite its efficacy, radiotherapy faces significant challenges in many low- and middle-income countries, where access to modern radiotherapy facilities and equipment remains limited [34]. These limitations lead to delayed treatments and poorer outcomes, especially in regions where early diagnosis is challenging and cancer detection occurs at later stages. In countries like Ethiopia and Haiti, the lack of access to radiotherapy services has resulted in higher cancer burdens and lower survival rates, further exacerbated by insufficient healthcare infrastructure [35, 36].

In high-income countries, advanced radiotherapy techniques such as intensity-modulated radiation therapy (IMRT) and image-guided radiotherapy (IGRT) have shown improvements in treatment precision, reducing side effects, and enhancing the quality of life for patients [37]. These techniques, however, are still inaccessible in many LMICs, where radiotherapy is often applied in less optimized settings, making it crucial to invest in expanding radiotherapy infrastructure and training healthcare providers in these regions.

The role of radiotherapy can also be influenced by the histopathological subtypes of gynecological cancers. For example, the aggressive nature of serous adenocarcinoma in ovarian cancer may require more intensive and extended radiation protocols to achieve optimal outcomes [38]. Moreover, tumor mutational burden (TMB) and molecular profiling are beginning to play a more significant role in guiding radiotherapy treatment. Patients with higher TMB might benefit from more tailored radiation approaches, potentially enhancing the effectiveness of therapy and minimizing side effects by targeting specific molecular pathways.

While radiotherapy remains a cornerstone in the treatment of gynecological cancers, especially in advanced and recurrent cases, its application must be optimized with an individualized approach, incorporating new technologies and molecular insights to improve patient outcomes. Furthermore, expanding access to radiotherapy in underserved areas is critical to addressing the growing global burden of gynecological cancers, particularly in LMICs. Efforts should focus on increasing radiotherapy infrastructure, ensuring equitable access to high-quality care, and integrating radiotherapy into a multidisciplinary approach for the management of gynecological cancers.

However, some limitations should be noted in this review as follows: In relation to the epidemiology and disease burden of gynecological cancers. First, the variability of the studies, regarding the study design, population, and methods used, may cause a problem of external validity. It was found that the studies

[DOI: 10.61186/ijrr.23.4.37]

differed by the number of participants, locations of origin and the types of gynecological cancers that were investigated; these differences could result in possible selection bias with respect to the effects documented.

Second, the majority of the studies reviewed in this paper were retrospective in design, which increases the risk of recall bias and hence inaccurate data collection. Also, the absence of follow-up data in many of the studies limits the ability to look at trends and outcomes of different forms of interventions and treatments in the long run.

One of the limitations is the scarcity of literature from some populations and regions of the world. For instance, low-income countries studies are limited and hence the results obtained from high resource countries may not be extended to these countries. This calls for more large scale, population-based research that would help to give a better picture of the global burden of gynecological cancers.

CONCLUSION

This review underscores the rising global burden of gynecological cancers, particularly in low- and middle-income countries, where disparities in access to screening and radiotherapy persist. Integrating molecular profiling and tumor mutational burden into clinical practice may enhance personalized treatment strategies. Expanding cancer care infrastructure and conducting region-specific epidemiological research are essential to improve outcomes and reduce global health inequities.

Acknowledgments

We would like to thank the Department of Oncology and Hematology at the People's Hospital of Leshan for institutional support during the development of this manuscript.

***Conflict of Interest*:** The authors declare that there are no conflicts of interest regarding the publication of this article.

***Funding*:** This study did not receive any specific funding from public, commercial, or non-profit organizations.

***Ethical Considerations*:** This article is a systematic review of previously published studies. No new studies involving human participants or animals were conducted by the authors. Therefore, ethical approval and informed consent were not required.

***Authors' Contributions*:** Y.F.: Proposed the research idea and designed the experimental plan; was responsible for data analysis and original draft writing. X.Z.: Performed experiments and collected data; participated in data analysis and revision of the paper. J.L.: Provided technical support and data verification; participated in the writing of the manuscript and the production of figures. All authors have read and approved the final version of the manuscript.

***AI Usage Disclosure*:** Artificial intelligence tools were used to assist in language editing, summarizing data, generating figure captions, and formatting the manuscript. All AI-generated content was carefully reviewed and revised by the authors to ensure scientific accuracy and integrity.

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[DOI: 10.61186/ijrr.23.4.37]

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[DOI: 10.61186/ijrr.23.4.37]