



Reproductive Problems in Adolescent and Young Adult Gynecology Cancer Survivors: A Systematic Review

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ABSTRACT

Adolescents and young adults with gynecology cancer are unique, especially in terms of their reproductive and sexual aspects. This systematic review aimed to identify reproductive problems in adolescent and young adult survivors of gynecology cancer. Articles from five databases were reviewed. PubMed, Taylor & Francis, Scopus, Science Direct, and Proquest, which were published in 2012–2023, 15–39 years of age, who had gynecology cancer and had completed cancer treatment. Biased risk assessment using Joanna Briggs Institute (JBI) tools. From the 1.167 articles, 12 were reviewed in this systematic review. Based on the results of the study, there were 4479 adolescent and young adult cancer survivors and 990 with gynecology cancer (cervical, ovarian, endometrial, pelvic, and vulva). The average age at diagnosis of cancer was 33,58 years old. Reproductive problems that occur in adolescents and young adults are sexual dysfunction, sexual activity, fertility, and psychosocial problems as a result of reproductive problems. Adolescent and young adult cancer survivors need information on reproductive issues and fertility maintenance after completing cancer treatment. Health professionals must focus on reproductive problems and counselling about long-term reproductive health among adolescent and young adult gynecology cancer survivors.

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ABSTRAK

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INTRODUCTION

Adolescents and young adult are the group 15-39 years old (National Cancer Institute, 2022; Smith & Olsen, 2018). More than 30 years of age, adolescents and young adults with cancer have not increased survival rates, and cancer is still the leading cause of death among the age groups of 15-24 years old and 25-39 years old (American Cancer Society, 2020). Cancer is a major problem among adolescents and young adults, prevalence worldwide of 19/100,000 population each year in adolescent and young adult (Atta et al., 2019). The prevalence of cancer in Indonesia, based on the age group of 15-24 years old is 0.47 per 1000 population and aged 25-34 years old is 1.21 per 1000 population (Badan Penelitian dan Pengembangan Kesehatan, 2019). One of the rising cancers is gynecology cancer, which occurs in 16% of women worldwide. Nearly 10% of women diagnosed with gynecology cancer are under the age of 40 or are still in the early adult development stage (NCCN, 2022). The proportion of female cancer patients who had been treated at Dr. Cipto Mangunkusumo was 63,3% and 1.73 times more than male patients, respectively. Most cancers are cervical cancer 15.80% and breast cancer (13.50 %) (Gondhowiardjo et al., 2021).

Adolescents and young adults with cancer in women are unique, especially in terms of sexual and reproductive health. This is related to the diagnostic and treatment procedures applied to gynecology cancer, which are very diverse, complex, and long. They will have problems with body image, sexual identity, and decreased reproductive ability, which will negatively affect their quality of life (Evcili & Bekar, 2020). The need for support for adolescents and young adults with cancer will be different from that for children or older adults. Because they are differentiated by disease categories, one is childhood cancer, and the other is adult cancer. Adolescence and young adulthood are a period of transition from children to adults (Ferrari et al., 2021; Smith & Olsen, 2018). Adolescents and young adults are concerned about physical appearance and self-existence, construct their identity, develop body image and positive sexual identity, separate from their parents, develop their involvement with friends of the same age, date, and begin to make decisions and life choices (Broholm-Jørgensen et al., 2022; Ham et al., 2022).

Women undergoing cancer treatments such as chemotherapy and radiation have a negative impact on fertility (Abelman & Cron, 2020). Young infertility is a major cause of distress among patients and their families (Mulder et al., 2021). Cancer treatments in women, such as chemotherapy and radiotherapy, are often associated with their impact on reproduction. Premature ovarian insufficiency (POI), infertility (Ojo et al., 2022), and inability to produce mature eggs for ovulation (Harzif et al., 2017) are major concerns for women undergoing cancer treatment and have a long-term impact on cancer survivors. This worsens emotional conditions, relationships, and sexuality (Harzif et al., 2019; Ojo et al., 2022).

Adolescents and young adults diagnosed with cancer at an advanced stage will experience early death from cancer because there is no hope of recovery, but they do not face the threat of death immediately after diagnosis or after completing active cancer therapy (Ham et al., 2022). The poor quality of the post-care phase in adolescents and young adulthood is one of which is counseling on reproductive health (Murphy et al., 2013). Adolescents and young adults feel uncomfortable discussing reproductive issues with health workers. Health workers also assume that adolescent and young adult cancer survivors are not interested in sexual activity during or after cancer treatment (Murphy et al., 2015; Murphy, Klosky, et al., 2013).

Adolescents and young adults may differ from other age groups related to reproduction, but their involvement in research is still very limited (American Cancer Society, 2020). Kim et al. (2016) studied 51 qualitative articles on adolescents and young adults with cancer and recommended adjustments to the type of cancer, type, and intensity of treatment. Although cancer at a young age presents similar challenges and problems, it has a different impact. Therefore, this systematic review aimed to identify reproductive problems in adolescent and young adult survivors of gynecology cancer.

METHODS

This systematic review aimed to identify reproductive problems in adolescent and young adult survivors of gynecology cancer. Format-based clinical questions Population, Interest, and Context (PICO). The steps in conducting a systematic review were adjusted to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist from Page et al. (2021). The inclusion criteria in the systematic review included non-experimental research articles (cross-sectional, observational study, or articles mixed method with observational study), article full text, and in English, a study with a sample of 15-39 years old gynecology cancer survivors who had completed primary cancer treatment.

Five databases were searched: PubMed, Taylor&Francis, Scopus, Science Direct, and Proquest. An article search was carried out by collecting and exploring articles published between 2012-2022 that reported reproductive problems in gynecological cancer survivors. A comprehensive article search was conducted. A search was also carried out using a list of references identified from articles obtained from the databases. Database searches were performed according to PICO combined with AND, OR Boolean operators, namely (gynecology cancer* OR gynecology neoplasms* OR female genital neoplasms*) AND (adolescent and young adult* OR emerging adult* OR youth*) AND (reproductive problems*OR sexual problems*OR reproductive burden*OR reproductive concern). The detailed search strategy is shown in Figure 1.

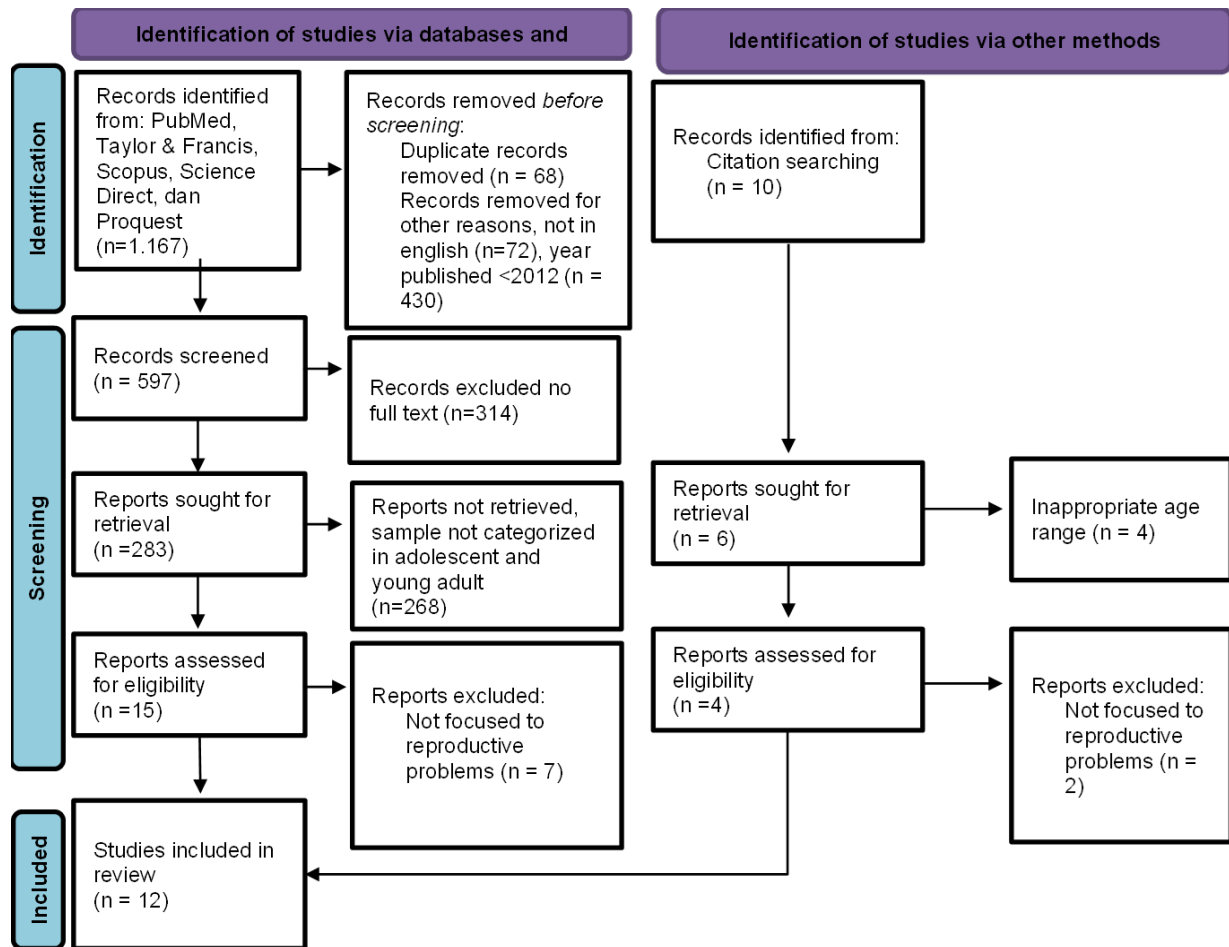


Figure 1. PRISMA flow diagram: selection process of articles

Process risk of bias for cross-sectional and cohort studies using the Joanna Briggs Institute (JBI) tool. The tool focused on three components: design, data collection, and analysis. There were questions to evaluate an article with yes, and no/unclear answer choices. Studies with high scores were indicated to have a low risk of methodological bias. Risk of bias is categorized as high risk of bias (1-3), medium risk of bias (4-6), and low risk of bias (7-9) (Harris et al., 2022). The rating score values of the risk of bias are displayed in Table 1. Data extraction included author's name, date of publication, country where research was conducted, research design, data source, data collection method, date of data collection, sample characteristics, findings, and quality of the article.

RESULTS

Characteristic of Respondents

A total of 4479 female adolescent and young adult cancer survivors and 990 female patients with gynecology cancer types (cervical, ovarian, endometrial, pelvic, and vulvar) were included. The average age at diagnosis of cancer from the 12 articles was 33.58 years. Survivors in the 12 studies included patients with cancer who had completed treatment for their primary cancer. The length of time spent as a survivor ranges from one day to 27 years. There were seven studies in which the data collection had been survivors of less than five years. The most common treatment

experienced by survivors was more than two therapy/combination therapies (49.70%-69.70%), chemotherapy (50%-78%), and surgery (64%-92.50%).

Reproductive Problems in Adolescent and Young Adult Survivors

Reproductive and fertility problems occurred in 82.7% of adolescent and young adult survivors, which was significantly higher than that of adolescents and young adults who had never been diagnosed with cancer ($p < 0.01$) (Furui et al., 2019). Gynecological cancer survivors experience moderate-to-severe reproductive problems (Young et al., 2019). Women with cervical and ovarian cancer experience ≥ 1 domain of sexual dysfunction. Problems with sexual dysfunction (interest in sexual activity) with OR 0.92; CI95% (0.59-1.43) (Wettergren et al., 2022). Sexual activity was significantly lower in middle-aged adults ($p = 0.0001$) in sexual activity. Comparing survivors aged ≤ 45 years and >45 years, sexual satisfaction, vaginal sexual function, and body image of survivors aged ≤ 45 years were significantly higher than those of survivors aged > 45 years ($p = 0.001$; $p = 0.001$; $p = 0.009$) (Bifulco et al., 2012). Women with reproductive cancer were significantly more dissatisfied with sexual activity than women with non-reproductive cancer ($p = 0.042$) (Mütsch et al., 2019). Reproductive problems may be related to the characteristics of cancer survivors during adolescence and young adulthood. Reproductive problems occurred in 68% of adolescent and young adult survivors undergoing chemotherapy (Furui et

al., 2019), aged 25-30 years ($p < 0.001$), and those who were not married ($p < 0.001$). Adolescent and young adult cancer survivors were also at high risk of moderate and high fertility disturbances (6.74 ± 1.96 ; mean \pm SD). Infertility can occur as a result of cancer therapy (Urech et al. 2018). Among adolescent and young adult cancer survivors, 9,6% experienced amenorrhea, 47.2% experienced oligomenorrhea, 38.4% experienced menstruation ≤ 7 days, and 20.2% experienced menstruation 60 days/year apart (Kim et al., 2021). Survivors aged ≤ 45 years were significantly more likely to experience menopausal symptoms than those aged >45 years ($p = 0.0001$).

Psychosocial Impacts Affecting Reproduction

Adolescent and young adult cancer survivors experience severe stress (Kim et al., 2021). Adolescent and young adult survivors undergoing chemotherapy or radiotherapy were more stressed than other cancer treatments (OR=5.55;95%CI 0.37-83.19). Cancer damage to body image affects interpersonal relationships, causing stress (Duan et al., 2021). The emotional function of survivors aged ≤ 45 years was significantly lower than that of survivors aged >45 years ($p = 0.03$) (Bifulco et al., 2012). There was no significant association between the stress experienced by adolescent and young adult survivors and decreased ovarian function in 311 survivors who had completed cancer treatment for >2 years.

Table 1. Study Characteristic

Author Country	Study Design, Data Sources, Data Collection Methods	Characteristic survivors	Findings	Quality Score
(Anderson et al., 2023) United States	<p>Cohort Study</p> <ul style="list-style-type: none"> - Women with cancer aged 15-39 years old, ≥ 18 years old at time of the study - Data sources from registers cancer North of Carolina, Northern California, and Southern California from 2004-2016 - Data collection was conducted from September 2018- November 2019 	<ul style="list-style-type: none"> - AYA cancer survivors (n=801), sample of gynecology cancer (cervical, endometrium, and ovaries) (n=117) - Median age (32 years old) and median age during collection enrollment (39 years old) - 40% of respondents diagnosed with cancer less than six years - 63% of respondents had a partner at the time of cancer diagnosis - 51% of respondents undergoing chemotherapy - 59% had never given birth before diagnosed with cancer, and 15% experienced infertility. 	<ul style="list-style-type: none"> - Women aged 35-39 (PR= 0.59; 95% CI, 0.41, 0.86) years old at diagnosis were less likely to become pregnant than those aged 15-24 years old. - Based on cancer characteristics, the type of cancer was significantly associated with pregnancy, survivors of gynecology cancer (PR=0.46; 95% CI, 0.32-0.67) were less likely to get pregnant than thyroid cancer survivors. - 85% of gynecology cancers discussed fertility and 25% received counseling from a fertility specialist. - Only 21% of women were pregnant <6 years of cancer diagnosis, 37% and 42% of women were pregnant within 6 to <10 years and >10 years of diagnosis - Fertility counseling with health professional or with fertility specialists from the diagnosis of cancer to the start of treatment is significant related to successful pregnancy (PR=1.74; 95%CI, 1.31-2.32). 	6 (Medium risk of bias)
(Bifulco et al., 2012) Italia	<p>Cross Sectional Comparative Study</p> <ul style="list-style-type: none"> - Survivors of gynecology cancer and breast cancer aged 18-65 years old. - Group A (young adults, ages 18-45 years old), group B (middle adults, ages 45-65 years old) - Stages I-II (uterus, cervix, and ovaries) - 1-4 years after cancer treatment - Data from cancer registers 2006 to 2010. 	<ul style="list-style-type: none"> - Young adult women (age 18-45 years old) (n = 106) with uterine cancer (n = 30), ovarian cancer (n=30), and cervical cancer (n=20). - 86.8% with stage one cancer, 74,5% undergoing surgery - The mean age for the young adult (42.8\pm2.2) - The mean distance between after cancer treatment is 32.7 \pm 11.9 months 	<ul style="list-style-type: none"> - Emotional functioning of young adults was significantly lower than those of middle adults (64.47\pm 21.15, $p = 0.03$) - Young adult sexual activity was significantly higher than middle adult (65.41\pm28.8 $p = 0.0001$) - Sexual satisfaction of young adults was significantly higher than middle adults (68.06 \pm25.6, $p = 0.0001$) - Body image of young adults was significantly higher than that of middle adults (47.98 \pm39.2, $p = 0.009$) - Young adult vaginal sexual function was significantly higher than middle adult (53.89\pm25.0), $p = 0.001$ - Young adult menopausal symptoms was significantly higher than middle adult (35.19\pm20.2), 	5 (Medium risk of bias)

Author Country	Study Design, Data Sources, Data Collection Methods	Characteristic survivors	Findings	Quality Score
(Furui et al., 2019) Japan	Cross sectional study - Adolescents and young adults aged 16-39 years old. - Survivors who have completed cancer treatment at least 12 months before it. - Data collection was conducted from June 2016 to November 2016 - Healthy group of adolescents and young adults recruited from the website	- Female survivors (n=32), survivors with gynecological cancer (n=7) - The current age of female cancer survivors diagnosed with cancer is 15-19 years old (28.3 ± 5.32). - The current age of female cancer survivors diagnosed with cancer is 20-24 years old with mean ± SD (33.4 ± 5.03).	<i>p</i> =0.0001 - Reproductive and fertility problems in adolescent and young adult survivors were higher than healthy adolescent and young adult (<i>p</i> <0,01). - 82,7% of adolescent and young adult experiencing reproductive and fertility problems - 68% of adolescent and young adult experiencing reproductive problems are undergoing chemotherapy	3 (High risk of bias)
(Kacou et al., 2021) d' Ivoire	Cross sectional study - Women aged <40 years old when diagnosed with cervical cancer - Data collection from July 2012- May 2018.	- Adolescent and young adults diagnosed with cervical cancer (n=40) - Mean age of survivor (34±4,95) years old - 58,84% of survivors are cohabitation and 23,07% are not married	- 52.40% of patients had malodorous vaginal discharge as the earliest symptom - Abnormal vaginal bleeding was the main complaint of 79.50% of women - Only 41% of patients had honored their completed treatment, of which 68.75% and 31.25% had received surgery and chemotherapy - 76.20% of cervical cancer survivors were at most stage IIA	6 (Medium risk of bias)
(Lam et al., 2020) California and Texas	Cross sectional study - Diagnosed with cancer at the age of 15-35 years old, aged 18-40 years old at the time of data collection - Completion of primary cancer treatment - The presence of at least one ovary - Study participants recruited between 2015 and 2018 who were nulliparous	- 413 nulliparous Adolescent and young adult survivors, gynecology cancer survivor (n=41) - The mean age (SD) of survivors at enrollment was 31.8 (4.9) years old, with a mean of 6.5 (4.4) years since cancer diagnosis. - Gynecology cancer survivor voluntary childless (26,8%) and 73,2% desires future children	- Survivors age 18-40 years desires future children compared with voluntary childless (<i>p</i> <0.001) - Older reproductive age of 36-40 years, compared with ages 25-35 years, had a threefold higher odds of voluntary childlessness (OR 2.97; 95% CI, 1.71-5.18) - age, sexual identification, gravidity, cancer treatment was not significantly associated with voluntary childlessness (OR 0.60; CI 95%;0.35-1.02)	6 (Medium risk of bias)
(Mattsson et al., 2020) Sweden	Mix methods- Cross-sectional study - aged 19-39 years old at time of diagnosis - having completed primary treatment - women diagnosed with gynecology cancer - diagnosis of gynecologic cancer between 2008 and 2016	- 207 adolescent and young adult gynecology cancer survivors - The median (range) age at diagnosis for the total sample was 35 (21-41) years old - women diagnosed with cervical cancer (n = 130) were 35 (25-41) years old, and 34 (21-41) and 38 (23-41) years old for women diagnosed with ovarian cancer (n = 57) and other diagnoses (n = 20), i.e., endometrial, pelvic and vulvar cancer. - Nearly half received multimodal treatment, (46.9%)	- The proportion of women with ovarian cancer (n = 23, 40.4%) who reported having children was lower than among women with cervical cancer (n = 91, 70.0%) - Unmet long-term supportive care needs (66,7%) and 80,7% women diagnosed with ovarian cancer described unmet needs. - Distress regarding sexuality and infertility issues that was not acknowledged by the health care team. Concerns regarding how to deal with sexual problems and how these problems affect a relationship. Need for follow-up care where partners were offered to participate actively.	4 (Medium risk of bias)
(Urech et al., 2018) UK, USA, Switzerland, Germany, Austria	Mix methods- Cross-sectional study - Women were ≥18 years old, had a cancer diagnosis within the last 10 years (and during their reproductive lifespan) - Women had a cancer	- 155 women survivors - Women with cervical cancer (n=38), uterine cancer (n=14) - 77.4% women survivors were informed by a health care professional about how cancer treatment might affect fertility	- (82.9%) women survivors stated that having a child was important, (75.4%) stated that it is difficult to imagine a life without children, and (76.0%) estimated being a parent as one of the most important things. - every cancer patient undergoing a treatment that might harm fertility	3 (High risk of bias)

Author Country	Study Design, Data Sources, Data Collection Methods	Characteristic survivors	Findings	Quality Score
	<ul style="list-style-type: none"> therapy potentially affecting the reproductive function - participants recruited in the English and German speaking countries - Duration of the study 1,5 years 	<ul style="list-style-type: none"> - 27.7% feared that infertility was the consequence of therapy - The mean (SD) age at diagnosis for the total sample was 35,89 ($\pm 7,92$) years, with a mean of 4,98 ($\pm 6,57$) years since cancer diagnosis. 	<ul style="list-style-type: none"> should be provided with the opportunity to preserve fertility (93,3%) - Only 29,9% women survivors having undergone fertility preservation - Risk for fertility difficulties between middle and high [6.74\pm 1.96; mean\pm standard deviation (SD)]. 	
(Wettergren et al., 2022) Sweden	<p>Cross-sectional study</p> <ul style="list-style-type: none"> - Young adults the first five years after being diagnosed with cancer - Women at the age of 18–39 years old who were diagnosed with cancer, during the period January 2016 through August 2017 	<ul style="list-style-type: none"> - 694 women with cancer, 495 days after diagnosis - Young adult with cervical cancer (n=190) and ovarian cancer (n=32) - The mean (SD) age at diagnosis for the total sample was 34,5 ($\pm 4,9$) years - Women cancer survivors had more children ($p < 0,001$), unemployed ($p < 0,001$) more than general population - Women with cervical cancer (80%) and ovarian cancer (97%) having undergone surgery 	<ul style="list-style-type: none"> - Women with cancer reported most problems with regard to lack of interest in sexual activity (45%), ability to reach orgasm (34%), satisfaction with one's sex life (22%), and vulvar discomfort (22 and 28%, clitoral and labial respectively) - Women with reproductive cancers reported more sexual dysfunction than the general population, lack of interest in sexual activity (48%) (OR 0.92; 95% CI, 0.59–1,43) and sexual dysfunction (66%) (OR 0.81; 95% CI, 0.54–1,22) 	6 (Medium risk of bias)
(Duan et al., 2021) China	<p>Cross-sectional study</p> <ul style="list-style-type: none"> - Adolescent and young adult at the age 15-39 years old, diagnosis with cancer - Recruited between March and October 2018 	<ul style="list-style-type: none"> - Total sample (n=809), women with cancer (n=483), gynecology cancer (n=93). - Majority of participants were between 36 and 39 years old (48.8%) and married (72.7%) - Majority of participants diagnosis with cancer < 3 months (30,5%). - Nearly half received multimodal treatment, (42,3%). 	<ul style="list-style-type: none"> - Adolescent and young adult underwent chemotherapy more likely to be distressed (OR 5,55;95%CI, 0,37-83,19) - Cancers could damage the patients' appearance and influence interpersonal relationships. 	4 (Medium risk of bias)
(Mütsch et al., 2019) Jerman	<p>Cohort study</p> <ul style="list-style-type: none"> - Age at diagnosis 18-39 years old - Diagnosis within the last 48 months. - Survivors are grouped into reproductive cancer and nonreproductive cancer - Instrument in this study, the life satisfaction questionnaire (FLZ) – sexuality scale (FLZ Sex), Changes in sexuality (FLZ-MC), Supportive care needs survey questionnaire (SCNS-SF34-G) – sexuality needs domain (SCNS-SF34 Sex) 	<ul style="list-style-type: none"> - Total sample (n=577), women survivors (n=424), reproductive cancer (n=201), gynecology cancer (n=51). - Women with reproductive cancer was significantly at age ($p < 0,001$), partnership ($p = 0,044$), and children ($p = 0,015$) compare with nonreproductive cancer - 78,6% of women with reproductive cancer receiving chemotherapy and 92,5% receiving surgery - The mean (SD) age at diagnosis for women with reproductive cancer was 32,32 ($\pm 5,02$) years 	<ul style="list-style-type: none"> - For females no significant differences between reproductive cancer and nonreproductive cancer were detected on the satisfaction with sexuality (FLZ-MC) scales ($p = 0,273$) - For females was significant differences between reproductive cancer and nonreproductive cancer were detected on the sexuality scale (FLZ sex) scales ($p = 0,008$) - Women were more likely than men to have lower sexual satisfaction scores ($b = -0.465, p \leq .001$) for the FLZ Sex scale and the FLZ-M Sex scale ($b = -0.229, p = .017$) 	7 (Low risk of bias)
(Kim et al., 2021) California	<p>Cross sectional study</p> <ul style="list-style-type: none"> - Females with cancer diagnoses between ages 15–35, ages 18–40 at study enrollment - completion of primary cancer treatment - presence of at least one ovary and - Adolescent and young adult survivors could enter the study from 1 	<ul style="list-style-type: none"> - Total sample (n=377), gynecology cancer (n=23) - The median age of participants was 34.0 years old (range 19–41) at a median of 6.0 years since cancer diagnosis - Half of participants (50.1%) were nulligravida 	<ul style="list-style-type: none"> - 9.6% of participants were amenorrheic, and 47.2% were oligomenorrheic - 38.4% experienced menses consistently more than or <7 days from prior pattern - 20.2% experienced menses at least 60 days apart in the prior year - 311 participants who were >2 years post-treatment, and there remained no significant association between stress and ovarian 	5 (Medium risk of bias)

Author Country	Study Design, Data Sources, Data Collection Methods	Characteristic survivors	Findings	Quality Score
(Young et al., 2019) United States	day to 25 years post-treatment. Cross sectional study - women with cancer diagnoses between the ages of 15 and 35 years old, ages 18 to 40 years old at study enrollment - completion of primary cancer treatment, and presence of at least 1 ovary - Reproductive concerns at study baseline were assessed with Reproductive Concerns After Cancer (RCAC) scale - participants as having moderate to high reproductive concerns if their overall RCAC score was >3	- Total sample (n=747), women with gynecology cancer (n=57). - The mean (SD) age at diagnosis for the total sample was 33,0 (±5,1) years, with a mean of 7,7 (±5) years since cancer diagnosis. - 44% of participants reported moderate to high overall reproductive concerns - 90% of participants received fertility counseling from a fertility specialist before cancer treatment, and 12% underwent a fertility preservation procedure. - Only 5% of gynecology cancer survivors received fertility counseling (P<0.001)	function outcomes - participant characteristics at cancer diagnosis were associated with undergoing fertility counseling, including older age ($P < 0.001$), cancer type ($P < 0.001$), and chemotherapy as part of cancer treatment ($P < 0.001$) - RCAC score for survivors who underwent fertility counseling was significantly higher than that of adolescent and young adult survivors who did not undergo counseling (3.06 [SD, 0.66] vs 2.85 [SD, 0.68]; $P = .001$). - Survivors without prior pregnancy or live birth, either before or after cancer, were also more likely to have moderate to high reproductive concerns ($P < .001$) than those with prior pregnancy or live birth. - Cancer type, age at diagnosis, radioiodine therapy, and surgery were not associated with reproductive concerns.	7 (Low risk of bias)

The Desire to Have Children

In two studies, 73.2% of adolescent and young adult cancer survivors wanted to have children in the future (Lam et al., 2020) and 82.9% stated that having children was important to them (Urech et al., 2018). A study by Young et al. (2019) found that more than half (74.8%) of the survivors did not want to give birth after a cancer diagnosis. Age, sexual identity, history of pregnancy, cancer treatment were not significantly related to voluntarily childless (OR=0.60; 95% CI 0.35-1.02). Adolescent and young adult cancer survivors ages 36-40 years were three times more voluntarily childless than those aged 25-35 years (OR=2.97; 95% CI 1.71-5.18) (Lam et al., 2020). The results of a study by Mattsson et al. (2020) showed that 59.6% of ovarian cancer survivors and 60% of uterine cancer survivors did not have children before being diagnosed with cancer. Results study of Anderson et al. (2023) found that more than half (59%) of the respondents had never given birth before being diagnosed with cancer. Only 21% of the women were pregnant for 10 years from the time of cancer diagnosis. Adolescent and young adult survivors who became pregnant after cancer treatment included live births (53%), miscarriage (22%), infertility (14%), pregnancy termination (7%), pregnancy (3%), and stillbirth or ectopic pregnancy (0.4%). Adolescent and young adult survivors aged 35-39 (PR= 0.59; 95% CI, 0.41, 0.86) at diagnosis were less likely to become pregnant from 15 to 24 years of age. Based on cancer characteristics, the type of cancer is significantly associated with pregnancy; survivors of gynecological cancer (PR=0.46; 95% CI, 0.32-0.67) are less likely to become pregnant than survivors of thyroid cancer (Anderson et al., 2023).

Need for Reproductive support

Four studies reported a need for reproductive support (Anderson et al., 2023; Mattsson et al., 2020; Urech et al., 2018; Young et al., 2019). Adolescent and young adult cancer

survivors did not receive fertility preservation services (88,2%) (Young et al., 2019); only 29.9% followed fertility preservation (Urech et al., 2018). Fertility counseling was not obtained in 81.1% (Young et al., 2019) and 66.7% (Mattsson et al., 2020) of adolescent and young adult survivors, respectively, diagnosed with cancer and during treatment. Only 5% of gynecological cancer survivors receive fertility counseling compared with other types of cancer (Young et al., 2019), and 80% of ovarian cancer survivors do not receive long-term support (Mattsson et al., 2020). Based on the type of cancer, 85% of gynecological cancer survivors discussed fertility, and 25% received counseling from a fertility specialist. Fertility counseling conducted with health professionals or fertility specialists from the diagnosis of cancer to the start of treatment was significantly associated with successful pregnancy (PR=1.74; 95% CI, 1.31, 2.32) (Anderson et al., 2023).

DISCUSSION

Reproductive problems occur in adolescent and young adult survivors (Bifulco et al., 2012; Furui et al., 2019; Kim et al., 2021; Mütsch et al., 2019; Urech et al., 2018; Wettergren et al., 2022; Young et al., 2019). The results of the study revealed reproductive problems, such as fertility disorders. Infertility occurs as a result of cancer treatment (Urech et al., 2018). The most common treatments experienced by survivors in this study were more than two therapies or a combination (49.70%-69.70%), chemotherapy (50%-78%), and surgery (64%-92.50%). Surgery is the most common primary treatment for cancer in adolescent and young adult survivors. Survivors of gynecological cancer are 86.8% stage one cancer (Bifulco et al., 2012) and 76.20% stage IIA cervical cancer (Kacou et al., 2021).

Reproductive problems occur in adolescent and young adult survivors undergoing chemotherapy (Furui et al.,

2019). Cancer treatments, such as chemotherapy, decrease ovarian follicles. Chemotherapy agents affect the growth of follicles in the ovaries due to the disruption of granulosa cell division caused by inhibition of DNA replication. Chemotherapy induces vascular damage and cortical ovarian fibrosis, resulting in local ischemia and a reduction in primordial follicles. In cancer patients, amenorrhea is a temporary effect of chemotherapy (Sodeifian et al., 2022). Cancer survivors who have completed cancer treatment experience amenorrhea, oligomenorrhea, menses ≤ 7 days, and menses 60 days/year apart (Kim et al., 2021). Survivors aged ≤ 45 years are significantly more likely to experience menopausal symptoms than those aged >45 years (Bifulco et al. 2012). A study by Wettergren et al. (2022) also showed that early menopause occurred in cervical cancer survivors because radiotherapy damaged the vaginal mucosa, causing the vagina to become fibrous, shortened, and dry (Wettergren et al., 2022).

Fertility disorders affect the possibility of pregnancy after a cancer diagnosis, even if these conditions may have occurred before a cancer diagnosis. Ovarian (59.6%) and uterine cancer survivors (60%) (Mattsson et al., 2020) did not have children before they were diagnosed with cancer. More than half (59%) of the adolescent and young adult survivors had never given birth before being diagnosed with cancer. Only 21% of the women were pregnant for 10 years from the time of cancer diagnosis. The cancer type is also significantly associated with pregnancy. Gynecological cancer survivors are less likely to become pregnant than thyroid cancer survivors are (Anderson et al. 2023).

In a study conducted by Urech et al. (2018), more than half (82.9%) of the survivors stated that having children was important. The results of this study are contrary to those of a study conducted by Young et al. (2019), which showed that more than half (74.8%) of survivors did not want to give birth after a cancer diagnosis and 98.5% did not want to adopt (Young et al., 2019). Survivors aged 36–40 years are three times more likely to be voluntarily childless than those aged 25–35 years (Lam et al., 2020). Not wanting to become pregnant can be caused by a possibly poor pregnancy outcome. Adolescent and young adult survivors who become pregnant after cancer include live births (53%), miscarriage (22%), infertility (14%), termination of pregnancy (7%), pregnancy (3%), and stillbirth or ectopic pregnancy (0.4%) (Anderson et al., 2023). Survivors are voluntarily childless because of the high risk of being passed on to children, or it is possible that children will have poor health conditions if born after suffering from cancer. Becoming a parent is not the primary goal for adolescent and young adult cancer survivors (Lam et al., 2020).

Decreasing ovarian function due to cancer treatment and having a long-term impact on women before the age of 40 will affect sexual health and function (Ayuandari et al., 2021; Hoven et al., 2021). Decreased sexual function is associated with decreased estrogen levels. Estrogen plays an important role in sexual desire, lubrication, and orgasm. Decreased estrogen levels as a result of decreased ovarian function can cause disturbances in sexual response and sexual desire (Codacci-Pisanelli et al., 2017). Cervical (61%) and ovarian cancer survivors (66%) experienced sexual dysfunction in more than one domain. Decreased desire for sexual activity and inability to orgasm (Wettergren et al., 2022). Women with reproductive cancer survivors were significantly dissatisfied with their sexual activity compared to women with non-reproductive cancers (Mütsch et al., 2019).

Female cancer survivors age range 25–30 years and not married have more severe symptoms (Young et al., 2019).

These results contradict those reported by Mütsch et al. (2019) and Bifulco et al. (2012). Older female survivors had significantly lower levels of sexual satisfaction (Mütsch et al., 2019). Sexual satisfaction and vaginal sexual function scores in survivors of gynecological cancer aged ≤ 45 years were higher than those in survivors aged >45 years (Bifulco et al., 2012). This difference can be influenced by marital status or the presence of a partner. Older women with reproductive cancer have more partners than younger women (Anderson et al., 2023; Duan et al., 2021; Kacou et al., 2021; Mütsch et al., 2019). Survivors of gynecological cancer who are >45 years of age also have a higher sexual activity score than those aged ≤ 45 years (Bifulco et al., 2012).

Survivors of gynecological cancer have been reported to have more psychological problems than physical problems due to cancer or cancer treatment (Brotto et al., 2008). The results of this study indicated that younger survivors of gynecological cancer have negative emotional and social impacts (Bifulco et al., 2012). The psychosocial impact on adolescent and young adult cancer survivors is related to demographic characteristics (gender, age, marital status, length of time being a survivor) and clinical characteristics (type of cancer and cancer treatment) (Bifulco et al., 2012; Duan et al., 2021). Females, younger adolescents, and young adults have a high level of stress (Duan et al., 2021). A decrease in the amount of estrogen during a decline in ovarian function causes disturbances in the sexual response and sexual desire. Sex hormones also have neurobiological functions; a decrease in the amount of these hormones causes anxiety in patients and disrupts neurovascular sexual responses (Codacci-Pisanelli et al., 2017). These results are in agreement with the results of a study (Mütsch et al., 2019) that found no difference in the psychological problems experienced by adolescent and young adult survivors with reproductive and non-reproductive cancers. There was no significant relationship between decreased ovarian function in 311 adolescent and young adult cancer survivors who had completed cancer treatment for >2 years (Kim et al., 2021). Regardless of the type of cancer, adolescent and young adult cancer survivors experience changes in body image, shape, and weight, which can reduce self-confidence (Sodeifian et al., 2022).

Adolescent and young adult cancer survivors are still not met with fertility counseling and fertility preservation (Mattsson et al., 2020; Urech et al., 2018; Young et al., 2019). There are some obstacles in providing fertility services to adolescent and young adult women with cancer from the patient's perspective, such as because fertility is not their main focus; they only focus on survival and cancer treatment. Obstacles from health workers include a lack of awareness and knowledge related to fertility (Berg et al., 2019). There is an unmet need for fertility preservation because the costs are very expensive and are not facilitated by health insurance (Anderson et al., 2023). Adolescent and young adult cancer survivors expect that every cancer patient receiving therapy that can affect fertility should receive fertility preservation (Urech et al., 2018). Survivors expect psychological services from professional health workers when treatment is finished, information regarding the long-term effects of surgery and medication, and distress due to sexuality and infertility problems that are not well understood by the team and not understood to deal with sexual problems and their impact on relationships (Mattsson et al., 2020).

STRENGTHS AND LIMITATIONS

This study is the first to address reproductive problems in adolescent and young adult women diagnosed with gynecological cancer. Different types of cancer cause different reproductive problems. This study has limitations due to the limited literature regarding adolescents and young adults with gynecological cancer. The number of samples with a diagnosis of gynecological cancer in the article is still very small, which can allow the impact not to be pathophysiological in gynecological cancer. Research places are still limited to America, Europe, Africa, and Asia (Japan and China), and the selected articles are only in English, so there is a risk of language bias (biased language).

CONCLUSIONS AND SUGGESTIONS

Cancer survivors in adolescence and young adulthood experience various reproductive problems. They are influenced by the characteristics of cancer survivors themselves. Differences in age range, marital status, and obstetric status affect various reproductive problems. Adolescent and young adult gynecological cancer survivors mostly require reproductive and fertility counselling. Younger survivors of gynecological cancer face the risks of infertility or subfertility, early menopause, and emotional disturbances. Survivors need support regarding reproduction, sexuality, fertility, and information about the late effects on cancer.

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ETHICAL CONSIDERATIONS

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of Data and Material (ADM)

The dataset used in this study is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's Contributions

All authors contributed to this project and article equally. RA took the lead in conceptualizing this review, analyzed, interpreted data, and drafted the final manuscript. YA and INR contributed to the initial conceptualization of the manuscript, assisted with establishing reliability for the review procedures, and contributed substantially to the editing of the manuscript. All authors have read and approved the final version of the manuscript for submission.

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