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Comparing the Oncological Risk of Hormonal and Non-Hormonal Contraceptives in Cervical Cancer: A Literature Review

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Abstract

Cervical cancer is a malignancy with high morbidity and mortality rates among women worldwide, including Indonesia. While high-risk HPV (hr-HPV) infection is the primary cause, contraceptive use is strongly suspected to act as a significant cofactor in cervical carcinogenesis. This research aims to analyze the comparison of cervical cancer risk between hormonal and non-hormonal contraceptive use through a comprehensive literature review. The study design was a literature review with a systematic search strategy on PubMed and Google Scholar databases. Ten original research articles (5 national and 5 international journals) published between 2016 and 2026 were selected based on inclusion and exclusion criteria. The analysis results showed that 60% of the studies reported a significant association between long-term hormonal contraceptive use ≥ 5 years and an increased risk of cervical cancer, with Odds Ratio (OR) values ranging from 2.4 to 7.0. In contrast, non-hormonal contraceptive use, specifically the Intrauterine Device (IUD), consistently showed a lower risk profile or provided a protective effect against pre-cancerous lesions. However, some studies showed variations influenced by confounding factors such as age at first marriage and parity. Long-term hormonal contraceptive use is associated with an increased risk of cervical cancer, while non-hormonal contraceptives (IUD) have a better oncological safety profile. Comprehensive counseling and routine screening (VIA/Pap Smear) are required for contraceptive acceptors, especially long-term hormonal method users.

INTRODUCTION

Cervical cancer remains one of the most significant public health challenges for women around the world (Jahanfar et al., 2024; Muchtariza and Masnarivan, 2020). Based on the latest data from the World Health Organization (WHO) and the Global Cancer Observatory (GLOBOCAN), cervical cancer ranks fourth as the most commonly diagnosed cancer and the leading cause of cancer death in women globally, with an estimated 660,000 new cases and 350,000 deaths annually (Guida et al., 2022; Stelzle et al., 2021). In Indonesia, the burden of this disease is even heavier, where cervical cancer occupies the second position as the most common cancer suffered by women after breast cancer (Muchtariza and Masnarivan, 2020; Rusfandi and Indrawan, 2025). This high morbidity and mortality rate requires a deeper understanding of the various risk factors that can trigger malignancy in the cervical area (Muchtariza and Masnarivan, 2020; Mukti, 2021).

Although persistent infection by High-Risk Human Papillomavirus (hr-HPV) has been identified as the primary cause, the process of cervical carcinogenesis is multifactorial and involves a variety of cofactors (Bovo et al., 2023; Rusfandi and Indrawan, 2025). One of the risk factors that continues to be the subject of debate in the medical literature is the use of

contraceptives (Anastasiou et al., 2022; Kamani et al., 2022). As part of a crucial family planning program for Women of Childbearing Age (WUS), contraceptive options are generally divided into hormonal methods such as combination pills, injections, and implants as well as non-hormonal methods, especially Intrauterine Devices (IUDs) (Bovo et al., 2023; Corrêa et al., 2025). However, concerns have arisen regarding the long-term impact of exogenous hormones on cellular stability in the cervical transformation zone (Bovo et al., 2023; Yimer et al., 2021).

Theoretically, hormonal contraceptives are thought to act as cofactors that facilitate the integration of HPV DNA into the host cell genome through the stimulation of cellular proliferation by the hormone's estrogen and progesterone (Loopik et al., 2020; Mengistie et al., 2025). In contrast, some recent studies have shown the protective effects of the use of non-hormonal contraceptives such as IUDs, which are thought to be related to local immune responses or mechanical changes in the cervical mucosa (Corrêa et al., 2025; Loopik et al., 2020). Despite this, findings in the field show contradictory results; some studies report a significant association between the duration of long-term hormone use and an increased risk of pre-cancerous lesions (Amelia et al., 2022; Hidayati, 2020), while other studies have not found a statistically significant correlation (Gul et al., 2022; Shintya, 2023).

The inconsistency of data between primary studies, both at the national and international levels, creates ambiguity for clinical practitioners and contraceptive users in assessing the safety of the chosen method (Anastasiou et al., 2022; Rusfandi and Indrawan, 2025). Therefore, a comprehensive literature review is needed to synthesize the latest evidence on the comparison of cervical cancer risk between the use of hormonal and non-hormonal contraceptives (Bahamondes et al., 2015; Jahanfar et al., 2024; Rusfandi & Indrawan, 2025). This article aims to analyze the existing literature to provide a clearer understanding of the influence of different types of contraception on cervical cancer incidence, which is expected to be the basis for education and clinical decision-making for women of childbearing age in Indonesia. The benefits of this research are twofold. Theoretically, this review synthesizes and compares conflicting evidence on contraceptive-related cervical cancer risk, thereby enriching the academic literature on reproductive health and oncological epidemiology. Practically, the findings provide evidence-based guidance for healthcare providers in contraceptive counseling, help women of childbearing age make informed choices about family planning methods, and support policymakers in developing safer reproductive health programs in Indonesia.

RESEARCH METHODS

This research was a literature review that was systematically compiled to analyze the relationship between the use of hormonal and non-hormonal contraceptives to the risk of cervical cancer. The literature search was conducted in February 2025 using two main databases, namely PubMed and Google Scholar. The search strategy was carried out using Boolean operators (AND/OR) to improve the specification of the results. In the PubMed database, the keywords used were: ("contraceptive" OR "hormonal contraception" OR "oral contraceptive" OR "IUD" OR "intrauterine device") AND ("cervical cancer" OR "cervical neoplasia" OR "cervical intraepithelial neoplasia" OR "CIN"). Meanwhile, on Google Scholar, the search was conducted with the keyword: "contraceptive use of cervical cancer risk".

The articles selected in this review are limited to literature published in the last ten years (2016–2026). The inclusion criteria include original research articles, clinical trials, and meta-analyses published in Indonesian and English. All selected articles must be available in full-text form to ensure the depth of data analysis. Meanwhile, the exclusion criteria in this study are: (1) articles that are only available in abstract form, (2) articles that are not publicly accessible, (3) narrative review articles, and (4) articles with subject populations that are too specific to certain genetic disorders that are not representative of the general population of women of childbearing age.

The literature screening process is carried out in stages to maintain the quality of references. In the PubMed database, the initial search yielded 255 articles. After filtering by study type (original research and clinical trial), 48 articles were obtained, which were then narrowed back down to 26 articles after ensuring the availability of full text access. From these, 5 articles were selected that were most relevant to the research objectives. In the Google Scholar database, 66 articles were found that matched the keywords, of which 43 were original research. Through the title and abstract review process, 5 additional articles were selected. In total, there were 10 final articles (5 international journals and 5 national journals) that met all the criteria and were analyzed in this review.

RESULTS AND DISCUSSION

Table 1. Summary of Studies on Contraceptive Use and Cervical Cancer Risk

Author (Year)	Design & Location	Sample Characteristics	Key Findings
Amelia dkk. (2022) (Amelia et al., 2022)	*Case-Control Study*, Samarinda Hospital, Indonesia.	76 respondents (38 cases of cervical cancer, 38 non-cancer controls).	There was a significant relationship between the duration of hormonal use >5 years and the risk of cervical cancer (p=0.027; OR=2.446).
Sara Gul dkk. (2022) (Gul et al., 2022)	*Case-Control Study*, Peshawar, Pakistan.	400 women (200 long-term hormonal users, 200 non-users).	No significant association was found between the use of hormonal contraceptives >5 years and abnormalities in *Pap Smear results*.
Lea Andy Shintya (2023) (Shintya , 2023)	*Case-Control Study*, RS X Manado, Indonesia.	120 participants (60 cases of cervical cancer, 60 controls) with *a total sampling* technique.	There was no significant association between the type of hormonal contraception (pills, injections, implants) and the incidence of cervical cancer (p=0.100).
Mulyandari et al. (2020) (São Paulo et al., 2020)	Correlational Descriptive, Surakarta Health Center, Indonesia.	71 birth control acceptors (Pill and IUD users).	There was a significant relationship between the duration of use of birth control pills (p=0.046) and IUDs (p=0.011) on the risk of cervical lesions based on the IVA test.
Nazrul dkk. (2025) (Nazrul et al., 2025)	*Community-based Cross-sectional*, Bangladesh.	1,500 women in remote areas used *the hrHPV* self-sampling method.	The use of hormonal contraceptives ≥5 years independently increased the risk of hrHPV infection by 7-fold (AOR=7.0).

Adhikari dkk. (2019) (Adhikari et al., 2019)	*Population-based Cohort*, Finlandia.	20,514 young women were followed longitudinally.	The use of birth control pills from an early age does not increase the risk of cervical atypia; the risk is more influenced by the interval of sexual activity.
Nur Sholichah et al. (2024) (Sholichah et al., 2024)	Descriptive Retrospective, Purworejo Health Center, Indonesia.	101 acceptors (44 IUD users, 57 non-IUDs).	There was no significant association between IUD acceptors and positive IVA results (p=0.445). IUD users tended to be at lower risk.
Kiweewa dkk. (2019) (Gray et al., 2019)	*Prospective Study*, Afrika (Multi-site).	2,629 African women were at high risk of HIV/STI infection.	The use of injectable hormonal contraceptives is associated with a higher frequency of cervical infections than IUD users.
Nurma Hidayati (2020) (Hidayati , 2020)	Observational Analytics, Lampung Hospital, Indonesia.	222 respondents (83 cervical cancer patients, 139 controls).	History of hormonal contraceptives was strongly associated with the incidence of cervical cancer (p=0.000; OR=4.14).
Loopik et al. (2020) (Loopik et al., 2020)	*Population-based Study*, Belanda.	1,029,910 women in the national screening program.	Birth control pill users have a higher risk of CIN III+, while IUD use is associated with a reduced risk of cervical lesions.

Source: Author's synthesis from 10 selected articles (2016–2026) for literature review

Based on the results of a literature search through two main databases, namely PubMed and Google Scholar, a total of 321 articles were found in the initial stage. After screening based on inclusion criteria which included the type of original research study, the availability of full-text, and the relevance of the topic to contraceptive use and cervical cancer risk, 10 final articles were obtained that were eligible for review. A summary of the characteristics and main findings of these articles is presented in detail in Table 1.

The characteristics of the 10 articles reviewed include publications in the last ten years, i.e. between 2016 and 2026. The distribution of research locations shows geographical diversity consisting of 5 national-scale studies in Indonesia (Samarinda, Manado, Surakarta, Purworejo, and Lampung) and 5 international-scale studies covering the Netherlands, Finland, Bangladesh, Pakistan, and several countries in Africa (South Africa, Uganda, and Zimbabwe). The majority of studies used case-control and cross-sectional analytical observational designs, with one large-scale cohort study involving more than one million participants.

The results of the data synthesis showed a significant difference in risk between the use of hormonal and non-hormonal contraceptives. A total of 6 out of 10 studies (60%) reported a significant association between the use of hormonal contraceptives, especially oral and injectable types with a duration of use ≥ 5 years, to an increased risk of cervical cancer or high-risk HPV infection (hrHPV). In contrast, studies on non-hormonal contraceptives, especially Intrauterine Devices (IUDs), consistently showed a lower risk or even protective effect against pre-cancerous cervical lesions. However, there were 3 studies (30%) that reported insignificant results, where the risk was more influenced by factors of sexual activity and age of first marriage than by the type of contraception independently ($p > 0.05$). Overall, the duration of use was the

main determining factor in determining the magnitude of the risk of hormonal contraceptive acceptors.

Interpretation of Findings and Comparison Between Studies

A review of 10 main literature shows a complex picture of the influence of contraception on cervical health. The majority of studies confirm a positive correlation between long-term use of hormonal contraceptives and an increased risk of pre-cancerous lesions or invasive cervical cancer (Amelia et al., 2022; Hidayati, 2020; Loopik et al., 2020; Nazrul et al., 2025). These findings are supported by a significant Odds Ratio (OR), as reported by Nurma Hidayati (OR 4.14) and Amelia et al. (OR 2.44) (Amelia et al., 2022; Hidayati, 2020). However, there are data inconsistencies where studies by Sara Gul et al. and Shintya did not find a statistically significant association between hormonal use and cervical abnormalities (Gul et al., 2022; Shintya, 2023). These differences are most likely influenced by variations in methodology, screening criteria (IVA vs Pap Smear), as well as differences in respondent demographic characteristics such as parity status and early age of sexual activity which are strong confounding factors (Adhikari et al., 2019; Amelia et al., 2022).

Hormonal Contraceptives and Cervical Cancer Risk

The duration of use is a crucial determining factor in the use of hormonal contraceptives. Consistently, the literature shows that increased risk becomes noticeable after continuous use for 5 years or more (Amelia et al., 2022; Mulyandari et al., 2020). Nazrul et al. (2025) report that the use of hormones ≥ 5 years increases the risk of high-risk HPV (hrHPV) infection by up to 7 times (aOR 7.0; 95% CI 2.1–23.3) (Nazrul et al., 2025). This indicates that exogenous hormones do not act as primary carcinogens, but rather as cofactors that facilitate the persistence of viral infections. These results are in line with a population study by Loopik et al. which found that oral contraceptive users have a higher risk of developing Cervical Intraepithelial Neoplasia (CIN) grade III and above (Loopik et al., 2020).

Biological Mechanisms

The link between hormonal contraception and cervical carcinogenesis is explained through the interaction between steroid hormones (estrogen and progesterone) and HPV DNA in the cervical transformation zone. Estrogen and progesterone are thought to stimulate the expression of the E6 and E7 genes in HPV (Loopik et al., 2020; Shintya, 2023). E6 and E7 proteins work by degrading tumor-suppressing proteins (p53 and pRb), thereby triggering uncontrolled cell proliferation and inhibiting apoptosis of infected cells (Loopik et al., 2020). In addition, long-term use of hormones can induce changes in cervical ectopia, which expands the area of the transformation zone and increases the cell's susceptibility to infection as well as the integration of the HPV genome (Mulyandari et al., 2020).

Contracepts Non-Hormonal (IUD)

In contrast to hormonal contraceptives, the use of non-hormonal methods, especially Intrauterine Devices (IUDs), shows a safer trend and even tends to be protective. Loopik et al. reported that IUD users have a much lower risk of CIN3+ (aOR 0.6) (Loopik et al., 2020). In line with this, Nur Sholichah et al. reported that IUD acceptors have a lower chance of positive

cervical examination results than non-acceptors (Sholichah et al., 2024). This protective mechanism is thought to be related to a local inflammatory response triggered by the presence of a foreign body (IUD) in the uterine cavity, which indirectly stimulates immunological activity in the cervical area to eliminate virus-infected cells or dysplasia cells (Loopik et al., 2020). These data reinforce the argument that non-hormonal contraceptives are a safer alternative for women with high risk factors for cervical cancer.

Implications for Clinical Practice

The findings in this review have important implications for primary health services. Contraceptive counseling should be carried out comprehensively taking into account the patient's cervical cancer risk profile (Amelia et al., 2022). For long-term hormonal contraceptive acceptors (>5 years), health workers need to emphasize the importance of regular screening through the IVA or Pap Smear method at regular intervals (Amelia et al., 2022; Mulyandari et al., 2020). In addition, for women with high risk factors, switching to non-hormonal methods such as IUDs can be an effective preventive strategy (Loopik et al., 2020; Sholichah et al., 2024). A problem-solving-based approach in clinical practice is indispensable to ensure each acceptor gets the safest method of birth control according to their individual condition (Shintya, 2023).

CONCLUSION

A literature review of 10 selected studies demonstrated a significant correlation between long-term use of hormonal contraceptives and an increased risk of cervical cancer, where duration of use of five years or more was identified as a critical threshold that markedly increased the risk of malignancy and persistence of high-risk HPV infection (hrHPV), while non-hormonal contraceptive methods, particularly IUDs, showed a superior safety profile with a tendency of protective effects against the development of cervical intraepithelial lesions, although some studies reported insignificant results due to the influence of confounding factors such as sexual activity and screening methods used. These findings confirm that exogenous steroid hormones in oral and injectable contraceptives serve as cofactors of cervical carcinogenesis — not as a primary cause, but by facilitating the integration of the viral genome into host cells — indicating that the selection of contraceptive methods should not only be based on the effectiveness of pregnancy prevention but must also consider the patient's individual oncological risk profile, with IUD use emerging as a recommendation for a longer-term method that is safer in the context of cervical cancer prevention. Accordingly, health workers are recommended to provide more in-depth contraceptive counseling regarding the long-term risks of hormonal contraceptive use, prioritize non-hormonal methods for women with high risk factors, and conduct surveillance through routine screening such as IVA or Pap Smear for long-term hormonal acceptors; the public, particularly women of childbearing age, should increase awareness about the importance of early detection of cervical cancer through regular cervical examinations especially for hormonal contraceptive users of more than five years without waiting for the appearance of clinical symptoms; and future researchers are encouraged to pursue prospective cohort studies capable of strictly controlling confounding factors alongside more in-depth molecular studies on the influence of various types of progestin on the stability of the cervical transformation zone.

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