

Review Article

Oral contraceptives and intrauterine devices as risk factors for breast and cervical cancers: a systematic review

Mary K. Murithi¹, Teresa K. Ogeto², Michael N. Walekhwa^{2*}, Richard K. Njunge³,
Micah K. Lagat¹, Zablon L. Malago³

¹Department of Pre-Clinical, School of Pharmacy, Kabarak University, Nakuru, Kenya

²Department of Biomedical Sciences, School of Medicine and Health Sciences, Kabarak University, Nakuru, Kenya

³Department of Pharmacology and Pharmacognosy, School of Pharmacy, Kabarak University, Nakuru, Kenya

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*Correspondence:

Dr. Michael N. Walekhwa,

E-mail: walekhwa@gmail.com

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ABSTRACT

Breast and cervical cancers have commandingly become major public health threats across the world. While studies have reported on the nexus between the use of oral contraceptives (OCs) and intrauterine devices (IUDs) as risk factors for breast and cervical cancers, there exists a paucity of explicit data on the nature of the association. Authors report the effect of oral contraceptives and the use of IUDs on the development of breast and cervical cancers. Several databases (Cochrane Library, Google Scholar and PubMed) were searched using well-specified criteria and a total of 15 papers selected. Meta-analyses, systematic reviews and studies that used cross-sectional designs were excluded from the review. Three and twelve cohort and case-control studies were reviewed respectively. Four of these studies reported an increased association between oral contraceptives and the risk of cervical cancer while nine showed positive correlation between oral contraceptives and risk of breast cancer. One study showed association between levonogestrel IUDs and risk of breast cancer while the other study did not show association between both levonogestrel and copper IUDs with risk of breast cancer. Use of copper IUDs was associated with diminishing risk of cervical cancer. Overall, use of oral contraceptives upsurges risk of breast and cervical cancers especially when used for longer periods of time. Further studies should therefore be done to understand the mechanisms of action of oral contraceptives and IUDs on the development of both cancers.

Keywords: Breast cancer, Cervical cancer, Intrauterine devices, Levonogestrel, Oral contraceptives, Risk factor

INTRODUCTION

The prevalence, effects and outcomes of cancer have made it a subject in every household across the world. It is the top cause of death among all non-communicable diseases. According to World Health Organization, there are 18.1 million new cases of cancer every year; out of which 9.6 million die.¹ In every five men and six women, at least one from the former and latter develops cancer in a lifetime. Out of every eight men and eleven women who develop cancer, at least one dies from each cohort. Among women, breast and cervical cancers are the most diagnosed. Annual diagnosis and demises for and due to

breast cancer are at 1.7 million and 521,900 respectively. There are 527,000 new cases of cervical cancer every year. This makes it the second most diagnosed and leading cause of death among women living in middle and low-income countries.²

While these worrying statistics have been exacerbated by an amalgam of social demographic dynamics; the use of contraceptives, modern and/or traditional has particularly been reported to be one of the focal culprits. The world today has 1.9 billion women within child bearing age.¹ Out of these, 1.1 billion are currently using some form of family planning. A total of 842 million are enrolled on

contemporary contraceptive methods while up to 80 million are using traditional methods.³ Sterilization is the most frequently used method universally. For instance, of the total number of women who used family planning methods in 2019 (219 million), 23.7% utilized sterilization.⁴ Three other methods that were commonly used globally include: male condom, intrauterine device (IUD) and the pill at 189 million, 159 million and 151 million respectively. Generally, 45.2% of those enrolled on family planning methods use long-lasting methods; 46.1% use short term methods and; 8.7% use traditional methods.³

Various studies have reported on the nexus between use of different contraceptives versus augmentation and reduction of cancer. For instance, Ginsburg et al.⁵ reported that oral and injectable hormonal contraceptives upsurges the risk of breast and cervical cancers while; consumption of oral pills only, bolsters development of breast but reduces the risk of developing ovarian and endometrial cancers. Elevated doses of estrogen included in the pills have been hypothesized to be responsible for development of breast and cervical cancer although; in some instances, women who used Depo-Provera had elevated occurrences of breast cancer cases.⁶ On the flipside, the use of non-hormonal IUDs reduces the development of endometrial and cervical cancers while it has an inert effect on development and/or reversal of breast cancer.⁷

The increased prevalence of cancer cases globally, obliges that the scientific community is more focal and explicit on which contraceptives reduces and augments which type of cancers respectively. This is especially true for developing countries where any form of neoplasia is likely to graduate into cancer due to wanton diagnostic capacity and; lack of well disseminated information on the importance of early diagnosis. In Kenya for instance, 77.6% of married women are enrolled on some form of modern contraceptive while 60.55% of women between 15-49 years of age practice some form of birth control.⁸ These kinds of statistics coupled with the much documented and worrying role of birth control methods on the development of cancer can only mean that information is clearer.

Authors reviewed several papers in order to make more focal the role of contraceptive use on either the risk of development or reversal of breast and/or cervical cancer.

Methods

This review was conducted with the guidelines obtained from Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) according to Moher et al.⁹

Search strategy

Peer-reviewed articles were searched in the Cochrane and PubMed databases using Google scholar as a search

engine. The articles considered in this review were based on their relevance to the effects of contraceptive use on the prevalence of breast and cervical cancers among women. The search strategy used was: ((Breast Cancer) OR (Breast Cancer AND Contraceptives) OR (Cervical Cancer AND Contraceptives) OR (Cervical Cancer) OR (Breast Cancer AND Risk Factors) OR (Cervical Cancer AND Risk Factors) OR (Contraception AND Breast Cancer) OR (Contraception and Cervical Cancer)).

Selection criteria

To identify the eligibility of the studies in determining the effects of contraceptive used on the risk of developing breast or cervical cancers among women, authors reviewed titles, year of publication, abstracts and study designs. Authors were interested in the prospective cohort and case-control studies published within the last 10 years (2010-2020). The search was also limited to English language and in case of any local dialect, a translated version of the study in English was considered. The quality of the studies enrolled in the current review was also based on the use of well-defined objectives, procedures, justified sample sizes, cases and controls in the study and valid statistical analysis used. Both systematic and meta-analysis review papers were excluded. After application of these criteria, authors ended up with 15 papers.

REVIEW OF LITERATURE

To understand the effects of oral contraceptives and IUDs on development of breast and cervical cancers, authors reviewed 15 papers as presented in Table 1.

DISCUSSION

Different papers reviewed demonstrated varying associations between use of contraceptives as a risk of development of breast and/or cervical cancer. For instance, some studies reported no association while others reported either increased or interestingly, reduced association. Authors discuss findings from various studies sampled on the basis of: type of contraceptive used (oral and intrauterine devices); type cancer (breast and cervical); type of study design and; a range of sociodemographic factors.

Oral contraceptive use as a risk of breast cancer

Two main oral contraceptives exist: combined oral and progestin only.¹⁰ Most papers reviewed assessed the effect of the combined oral contraceptives (COCs) on development of both cervical and breast cancers. Authors report incredible blend of findings from various studies. For instance, Mørch et al, Rosenberg et al, Kotsopoulos et al, Roy et al, Bardaweel et al, Urban et al, and Vaisy et al, demonstrated a positive association between COCs and risk of breast cancer while Poosari et al, and Karim et al, reported inert association.¹¹⁻¹⁹ One thing that explicitly

stands out from the various papers reviewed is that regardless of the study design used, there seems to be a

running inert and positive trend between low and high sample sizes with reported associations respectively.

Table 1: Review of Literature from Selected Studies.

References	Type of cancer	Type of contraceptives	Study design	Methodology	Findings
1 ¹⁸	Breast	OCs	Prospective cohort	The number of participants recruited for the study was 11 414 Thai women. Study population was recruited starting from 1990 to 2001 after which follow up was done until December 31 st 2011. During this period 70 breast cancer cases were histologically confirmed. Emerging breast cancer cases were extracted from registry report. Use of hormonal contraceptives and breast cancer risk association was determined.	There was non-significant 1.31 times increase in breast cancer in women with a history of hormonal contraceptives use (95% CI, 0.65-2.65). There was no association between the type of hormonal contraceptive and breast cancer risk (Oral contraception: HR=1.35, 95% CI, 0.65-2.78; injection contraception: HR=1.25, 95% CI, 0.56-2.80). There was also no association between duration of hormonal contraceptives use to the risk of breast cancer. Similarly, there was no association between age at first use of hormonal contraceptives and breast cancer. It was noted that the HRs in women younger than 50 years and older than 50 years were 0.86 (95% CI, 0.30-2.45) and 1.91 (95% CI, 0.75-4.88) respectively.
2 ¹¹	Breast	IUD and OCs	Prospective cohort	A total of 1,797,932 women residing in Denmark aged 15 to 49 years between January 1, 1995 and December 31, 2012 constituted the study population. Breast cancer cases reported within the study period were 11, 517. Follow up was done up to the point of either breast cancer, or death or emigration as recorded in the registry, attainment of 50 years or end of follow up period. An update on hormonal contraception was obtained during the follow up period. It was assumed that levonorgestrel intrauterine device (LNG _{IUD}) was used for four years. Primary invasive cancers were identified from the Danish registry. Current and recent use as well as duration of use of the contraceptive in association with breast cancer risk was determined.	Current and recent use of hormonal contraceptives increased the rate of breast cancer (RR _{adjusted} 1.20, 95% CI, 1.14 to 1.26). Increased duration of using contraceptives increased the risk of breast cancer. Use of hormonal contraceptives for <1 year was RR _{adjusted} 1.09 (95% CI, 0.96 to 1.23) while use for >10 years was RR _{adjusted} 1.38 (95% CI, 1.26 to 1.51) (p=0.002) When adjusted for estrogen, breast cancer risk associated with use of combined oral contraceptives reduced. However, for gestodene products, the relative risk remained high (p=0.003) The effect of LNG _{IUD} to breast cancer risk was RR _{adjusted} 1.21 (95% CI, 1.11 to 1.33)
3 ¹²	Breast	OCs	Prospective	Study population consisted	Ever use of OCs showed a

				cohort	of 53,848 African American women aged between 21 to 69 years diagnosed with incident breast cancer in the period of March 1995 to 2007. 789 cases with confirmed receptor status and used oral contraceptives were used as cases. Follow up was done until time of diagnosis, loss of follow up, death or end of study.	strong association with ER-/PR- breast cancer (IRR, 1.65; 95% CI, 1.19-2.30) compared to that of ER+/PR+ (IRR, 1.11; 95% CI, 0.86-1.42). Increased duration of oral contraceptives among recent users increased the risk of ER-/PR- breast cancer (IRR 1.97 95% CI, 1.21-3.20)
4	²⁰	Breast	OCs	Case-control	This study was done between January 2007 and December 2013. Japanese women aged 20-69 years were included. 155 were cases diagnosed with breast cancer while 12, 223 were controls not diagnosed with breast cancer. Questionnaires and patient charts were used to investigate ever use, period of use and type of OC. Past, present and never use of OCs was also investigated.	Although not statistically significant, there was a negative association of use of OCs in premenopausal women with risk of breast cancer (OR 0.45; 95% CI 0.22-0.90). Similar to past use, present use of OC was also negatively associated with breast cancer (OR 0.51; 95% CI 0.27-0.96)
5	¹³	Breast	OCs	Case-control	Case subjects constituted 2492 BRCA1 mutation carrier women diagnosed with invasive breast cancer while the matched control subjects were 2492 BRCA1 mutation carriers who had never been diagnosed with breast cancer. The association of breast cancer risk with use, subject age and duration of use of oral contraceptives was determined.	Women who started using oral contraceptives before 20 years of age had an increased risk of breast cancer (OR 1.45; 95 % CI 1.20-1.75; p=0.0001) as well as those between 20 and 25 years (OR 1.19; 95 % CI 0.99-1.42; p=0.06). Initial use of oral contraceptives before 20 years increased the risk of breast cancer irrespective of the duration of use (p=0.003). There was an increased association between use of oral contraceptives and breast cancer diagnosis before age of 40 (OR 1.40; 95 % CI 1.14-1.70; p=0.001); Noteworthy, there was a significant 20% reduction in current OCs use (OR 0.80; 95% CI 0.66-0.97) and a significant 38% increased breast cancer risk in women who had stopped OCs in the previous five or more years (OR 1.38; 95% CI 1.18-1.61).
6	³¹	Breast	OCs	Case-control	798 women with contralateral breast cancer (CBC) and 1398 controls of women with unilateral breast cancer were diagnosed between 01/01/1985 and 31/12/2000. Analysis of the association between the use of OCs and CBC with ³¹ / ₂ mutation carriers was done.	109 and 72 women had BRCA1 and BRCA2 mutations respectively. There was no association between use of OCs with CBC risk among non BRCA1/2/ mutations (RR=0.87; 95% CI=0.66-1.15) or BRCA2 carriers (RR=0.82; 95% CI=0.21-3.13). On the other hand there was non-

					significant association between total use of OCs, use of OCs for 5 years before age of 30 and before first term full pregnancy, with CBC risk in BRCA2 mutation carriers (RR=0.82; 95% CI=0.21-3.13). However there was significant association between OCs use and CBC BRCA1 mutation carriers (RR=2.38; 95% CI=0.72-7.83).
7	21	Breast	IUD and progestin only pills	Case control	<p>5113 breast cancer cases diagnosed between January 2000–December 2007 and 20,452 population based controls in Finland and Germany were recruited. Ever-use and current use of Levonogestrel intrauterine device (LNG_{IUD}) and that of Copper intrauterine device (CU_{IUD}) were analyzed. Comparison of use of different contraception methods namely (LNG_{IUD}), progestin only pills, injections, non-use of hormonal contraceptives was analyzed.</p> <p>There was no association between risk of breast cancer and ever use of (LNG_{IUD}) (OR_{adjusted} 1.04 (95% CI, 0.93-1.17) and (CU_{IUD}) (OR_{adjusted} 0.99 95% CI, 0.88-1.12) and in present users at the point of diagnosis there was also no association (OR_{adjusted} 0.85 95% CI, 0.52-1.39). Overall there was no significant increase in breast cancer to the use of either (LNG_{IUD}), progestin only pills, injections and non-use of hormonal contraceptives.</p>
8	19	Breast	OCs	Case control	<p>The study was carried out in Saudi Arabia. It constituted 192 women (92 as cases and 100 as controls), aged between 30 and 65 years. Both questionnaires and medical reports containing oncologic data were used to collect data. Association between duration of use of oral contraceptives and incidence of breast cancer was analyzed. Age at breast cancer onset was correlated to age at start of oral contraceptives.</p> <p>Overall there was no association between OCs use and breast cancer (OR=0.276, 95% CI 0.092-0.829, p=0.524). Long term use of OCs showed an association with increased breast cancer risk (OR=0.297, 95% CI 0.158-0.557, p=0.001). Use of OCs for 10 years or more showed association to risk of breast cancer (OR=0.282, 95% CI 0.095-0.835, p=0.02). The starting age of use of OCPs did not influence breast cancer risk (p=0.452) nor the age at diagnosis (p=0.074).</p>
9	14	Breast	OCs	Case control	<p>Study included Bengalee female participants (108 cases and 120 age matched controls) aged between 30-72 years were included. Data on reproductive aspects, medical history and oncology was obtained from medical records. Association between ever use of OC to never use was analyzed.</p> <p>The risk of breast cancer in ever use of OC was 2.77 times compared to the non-users (OR=2.77, 95% CI 1.63-4.71, p<0.0001). When the period after discontinuing use of OCs is long the risk of developing breast cancer diminishes. Women who had stopped using the pills for 10 years or more did not show any increased risk.</p>

10	15	Breast	OCs	Case control	Study used 450 Jordanian women (225 cases and 225 controls) aged 18 to 65 years. Association between risk of breast cancer and OCs was determined.	When used regularly, OCs were found to increase breast cancer risk (OR _{adjusted} =2.25, 95% CI 1.34–2.79; p=0.002), However, there was no association between the length of using the OCs to the breast cancer risk (p>0.05).
11	24	Cervical	OCs, IUDs	Cohort Nested case-control	The European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study participants were 308, 036 women. 261 invasive cervical carcinoma (ICC) and 804 cervical intraepithelial neoplasia grade 3 (CIN3)/ carcinoma in situ (CIS) patients were identified. For the nested case control study, there were 609 cases of whom 184 had ICC and 425 had CIN3. 1218 controls were recruited. The factors analysed were; Use and duration of OC, time since first and last use among OC users. Never and ever use of intrauterine device (IUD) was also analyzed.	There was an increased risk of CIN3/CIS (HR=1.6 95% CI, 1.2-2.2) and ICC (HR=1.8 95% CI, 1.1-2.9) with increase in duration of oral contraceptive use. In the nested case control study, ever use of IUDs reduced the risk of ICC (OR=0.6 95% CI, 0.3-1.2). This was not statistically significant.
12	28	cervical	IUD	case-control	17,559 cases and 87, 378 controls women of age 18–49 participants were recruited between 1996 and 2014. 1,657 and 7925 IUD users were identified among the cases and controls respectively. recent IUD use was defined by one month or more prior to diagnosis within the 18 months of study. Parameters adjusted were; sexually transmitted infection, smoking, HPV vaccination, hormonal contraceptive use, parity, race and number of outpatient healthcare system visits was adjusted.	There was an association between use of LNG- IUD and cervical intra epithelial neoplasia 2+ (CIN2+) [RR 1.18 (1.08-1.30), p<0.001]. However, there was no association between CU-IUD and CIN2+ [RR 0.88 (0.75-1.04), p=0.13]. There was no association between use of IUD and CIN3+ [RR 1.02 (0.93-1.11), p=0.71].
13	23	Cervical	Hormonal	case-control	Total number of participants was 116 (58 cases and 58 controls) sampled between Jan-July 2009. Age, menarche, menopause, age of first marriage, parity, spouse's smoking status, hormonal contraception use, type of hormonal contraception, duration of hormonal contraception, IUD (intra uterine device) contraception use and duration of IUD	The study found out that parity and the length of period of hormonal contraception use increased the risk of cervical cancer. The duration of hormonal use was also found to increase the risks of cervical cancer. Women who had used hormonal contraceptives for 1-4 years were two times at risk (OR _{adjusted} ; 2.06 95% CI 0.84-5.34 p= 0.113) and those who had used contraceptives for a period of 5-25 years were 4.5

				contraception data was collected. Odds ratios were calculated.	times at risk of developing cervical cancer than those who have never used hormonal contraceptives (OR _{adjusted} ; 4.48 95% CI 1.73-11.56 p=0.002.
14	16	Cervical and Breast	OCs	Case-control	<p>The breast cancer patients had 1.66 times (OR 1.66, 95% CI 1.28-2.16, p<0.001) the odds to controls of having used either injectable or oral pills.</p> <p>There was an association of use of oral contraceptives only to breast cancer risk (OR 1.57, 95% CI; 1.03-2.40, p=0.04).</p> <p>Women who had previously used either oral or injectable contraceptive or both for the past 10 years were more likely to develop cervical cancer than those who had never used a contraceptive (OR 1.38 95% CI (1.08-1.77, p=0.01).</p> <p>The association of cervical cancer risk to use of oral contraceptives only was (OR 1.01 95% CI; (0.66-1.56, p=0.96).</p>
15	17	Cervical and Breast	OCs	Case – control	<p>The odds of developing cervical cancer for those with a history of contraceptive use was 3.72 95% CI; (1.84-5.11) while the odds of developing breast cancer was 2.11 95% CI (0.46-3.33).</p> <p>The odds of developing cervical cancer was 5.2 95% CI; (2.28-11.8) when the duration of use of oral contraceptive use was more than 97 months.</p> <p>The odds ratio of breast cancer to controls was 6.47 95% CI; (2.46-17.4) for those who had started using oral contraceptive pills after 30 years and 1.99 95% CI; (1.20-3.30) for those who started after 25 years.</p> <p>The odds of developing breast cancer for those who had used high-dose oral contraceptive pills was 2.28 95% CI; (1.13-4.57) while for low-dose oral contraceptive pills was 1.98 95% CI; (1.16-3.38).</p> <p>There was no significant relationship between age at first use of contraceptive and type of contraceptive and cervical cancer.</p>

Interestingly, Ichida et al, documented negative correlation between use of COCs and risk of breast cancer.²⁰ This can possibly be attributed to the ratio of cases to controls used in this particular study which was 1:79. Unlike in this study, the ratio of cases to controls in all other studies was either 1:1, 1:2 or 1:4. Therefore, the negative association reported may not actually be valid owing to the case control ratio used.

With regard to age of onset of oral contraceptive use versus risk of breast cancer, there are conflicting reports from different scholars. While Kotsopoulos et al, reported an increased risk of breast cancer if the subject started using oral contraceptives before 25 years of age; Vaisy et al, on the other hand, reported an increased risk for subjects who enrolled on oral contraceptives after 30 years of age.^{13,17} However, Poosari et al, and Karim et al, reported no associations at all.^{18,19} The duration of oral contraceptive use was reported to either have an association with risk of breast cancer or no association at all. For instance, Rosenberg et al, Karim et al, Vaisy et al, and Mørch et al, documented an association between increased duration of use of oral contraceptive and risk of breast cancer while Poosari et al, and Bardaweel et al, reported existence of no association.^{11,12,15,17-19} Some studies profiled the correlation between the period after cessation of oral contraceptive use and risk of breast cancer. Roy et al, opined that the longer the duration after cessation of contraceptive use the lower the risk of breast cancer.¹⁴ This finding surprisingly contradicts with that of Kotsopoulos et al, which reported that the longer the period after cessation of contraceptive use the higher the risk of breast cancer.¹³

Mørch et al. sought to understand the hormone that was more associated with the risk of breast cancer among subjects enrolled on COCs.¹¹ To achieve this, they adjusted for estrogen and established that the risk of breast cancer was reasonably reduced. This finding is coherent with that of Dinger et al, which reported no correlation between progestin only contraceptive and risk of breast cancer.²¹ Particularly, Mørch et al, noted that the relative risk for breast cancer remained high for gestodene products.¹¹ An interesting observation that could be attributed to that of Catherino et al, which associated gestodene with stimulation of breast cancer development through an oestrogen receptor mediated mechanism.²²

Oral contraceptive use as a risk of cervical cancer

Four papers reported associations between COCs and risk of cervical cancer.^{16,17,23,24} All these studies reported positive association between duration of oral contraceptive use and risk of cervical cancer. While the risk of cervical cancer is eminent among all subjects enrolled on COCs, those who use it for relatively longer periods of time have an even higher risk. Both scientific and conventional explanations suffice for this scenario. For instance, in 2017, Chagas et al, reported a possible

relationship between oral contraceptives and cervical hyperplasia while Gao et al, reported that elongated exposure to OCs had an impact on expression of differentially expressed genes in cervical cells which are thought to excite the process of cervical cancer development.^{25,26} Conventionally, Bassuk and Manson, associated women enrolled on OCs to the likelihood of indulgence in unprotected coitus which may promote the transmission of Human Papilloma Virus (HPV), a major risk factor of cervical cancer.²⁷ Vaisy et al, documented that there exists no relationship between age at first use and type of OCs and risk of cervical cancer.¹⁷

Intrauterine device use and risk of breast cancer

Two studies reported on the association between IUD use and the risk of breast cancer.^{11,21} Mørch et al, however, profiled the levonogestrel IUD use and reported positive associations while Dinger et al, studied the use of both levonogestrel and copper IUDs and interestingly, reported no associations.^{11,21} What is worth to note, is that the study by Dinger et al, powered the odds ratio (OR) at 1.5 as compared to that of Mørch et al, which found the risk ratio (RR) between the two variables to be at 1.2.^{11,21} It is not clear whether the high OR used by Dinger et al, could be the reason why there was no association between IUD use and risk of breast cancer as per this study.²¹ Whether the duration of use of IUD has an association with risk of breast cancer is yet to be well profiled.

Intrauterine device use and risk of cervical cancer

Use of copper IUDs had reduced association with cervical cancer and zero association with cervical intra-epithelial neoplasia 2 (CIN2) and cervical intra-epithelial neoplasia 3 (CIN3). Whereas that of levonogestrel IUDs slightly increases the risk of CIN2 but showed no association with CIN3 and cervical cancer.²⁸ In 2017, Roura et al. reported existence of an insignificant reduced risk of cervical cancer among subjects using IUDs a finding that is coherent with that of Cortessis et al.^{24,29}

Interestingly, Castellsagué et al, had earlier reported a strong and statistically significant inverse correlation between use of IUDs and the risk of cervical cancer.³⁰ Occurrence of a low grade, long-lasting and sterile inflammation which boosts the capacity of localized cervical immunity may be the reason that informs this association. What is more is that the device may also have capacity to create a non-conductive environment for the survival of HPV.

CONCLUSION

In the current review, authors conclude that the oral contraceptives increase the risk of breast and cervical cancer. Notably, copper IUDs has zero and reduced association with breast and cervical cancer respectively while the long use of COCs increases the risk of breast

and cervical cancer. Finally, levonogestrel IUDs slightly increases the risk of breast cancer and cervical intra-epithelial neoplasia 2 (CIN2).

Recommendations

In the light of the discussions aforementioned, further studies should be done to understand specific mechanisms of action of oral contraceptives and IUDs in the process of development of breast and cervical cancer. Clinicians should also provide adequate information to prospective candidates on the association between use of oral contraceptives and IUDs and the risk of breast and cervical cancer. This will enable them to make informed choices.

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