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Original Article

Obstetrics and Gynaecology Section

Association of Intrauterine Device (IUD) and Cervical Neoplasia - A Study in a Poor Nigerian Population

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ABSTRACT

Introduction: Intrauterine Device (IUD) is a contraceptive method used by women of reproductive age group. However, there are conflicting reports on the association between IUD and cervical neoplasia. These controversies may further hamper the poor uptake of modern contraception in Nigeria.

Aim: This study was therefore aimed at evaluating the association between IUD and cervical neoplasia.

Materials and Methods: This was a case control study in which Pap smear results of 156 participants on IUD were compared with those of 156 non-users of modern contraception. The participants who were found to have abnormal cervical smear cytology results were further subjected to colposcopy. Biopsy specimens for histology were collected from the participants with obvious cervical lesions or those with suspicious lesions on colposcopy. The results were analysed with descriptive and inferential statistics at 95% level of confidence.

Results: Seven (4.5%) and 2(1.3%) of participants using IUD had Cervical Intraepithelial Neoplasia (CIN) 1 and CIN 2 respectively. Also, 5(3.2%) and 1(0.6%) of non-users of modern contraception had CIN 1 and CIN 2 respectively. The prevalence of cervical neoplasia among all the participants was 4.8%. Although, the proportion of women who had CIN was more among participants using IUD than non-users of modern contraception, the difference was not statistically significant.

Conclusion: There was no significant association between IUD and cervical neoplasia in this study.

Keywords: Copper T380A, Colposcopy and biopsy, Cervical intraepithelial neoplasia, Nigeria

INTRODUCTION

Intrauterine Device (IUD) is one of the contraceptive methods used in Nigeria. It accounted for 56.67% and 25.5% of contraceptive use in Nnewi, South-East Nigeria and Port Harcourt, South-South Nigeria respectively [1,2]. The mechanism of action of IUD is by interfering with sperm survival and motility thus preventing fertilization and implantation [3]. There have, however, been conflicting reports on the association between IUD and cervical neoplasia. A study in India on the microbial and cytopathological study of IUD users showed that cervical epithelial lesions were found in IUD users but none in controls [4]. Another report from India showed that the incidence of cervical neoplasia increased with increasing duration of IUD use, regardless of whether the devices had been changed [5]. However, there was no comparison with the general population who never used IUD in that report. More so, a study of 3,374 Indian women who used different modes of contraception showed highest incidence of neoplasia among clients using IUD with high copper content. However, the accumulated follow-up data revealed that the CuT380A device was a promising IUD for future use in the light of its low incidence of neoplasia determined during its use for up to 5 years [6].

A multicentre study in United States of America (USA) showed that a protective effect against invasive cervical cancer was observed for copper-containing IUDs but not for inert devices [7]. Another study in USA showed that the use of IUD did not appear to increase the risk of neoplasia and it was also found that IUD use was associated with a decreased risk of endometrial neoplasia but it remained unclear whether the association was causal [8]. In Hungary, a 10 year follow-up study on the pre-malignant and malignant cervical pathologies among inert and copper-bearing IUD users, showed that the copper-bearing IUDs were not associated with a significantly higher risk of cervical cancer compared to the inert IUDs [9]. This study however lacked respondents who never used any form of modern contraception as controls. A study in Israel revealed that the use of IUD did not increase the incidence of squamous intraepithelial lesions [10]. But this was a retrospective study and so, adequate measures were not taken to control for confounding factors.

A report from Malaysia showed that 14 women (4%) on IUD had cervical intra-epithelial neoplasia (CIN). The participants with low-grade squamous intraepithelial lesion were reverted to normal after 6 months removal of IUD [11]. However, there was no proper control with non-users of modern contraception in this study. A colposcopic case-control study of cervical squamous intraepithelial lesions in women with anogenital warts revealed that CIN was strongly associated with current IUD usage and coitarche under 16 years of age [12]. Also the study on the Actinomyces-like structures and their association with IUD, pelvic infection and abnormal cervical cytology, showed a significant increase in cervical epithelial abnormalities in the cervical smears [13]. The drawback of this conclusion is that it was an incidental finding and therefore no proper matched controls were provided.

A review by the International Agency for Research on Cancer and Institut Català d'Oncologia research programme on HPV and cervical cancer, showed a strong inverse association between ever use of IUDs and cervical cancer. A protective association was also noted for squamous-cell carcinoma, adenocarcinoma and adenosquamous carcinoma. However there was no association among HPV-positive women. This study suggested that IUD use might act as a protective co-factor in cervical carcinogenesis [14].

Similarly, the New Zealand cohort study on the risk of cervical neoplasia in users of oral contraceptives, IUD or depot-medroxyprogesterone acetate showed no difference in risk of cervical neoplasia among women using these three methods of

contraception if the confounding factors were taken into account [15]. However, women on no form of modern contraception were not involved in this study. A case- control study by the authors, of which this study was part of, showed no significant association between hormonal contraceptives and cervical neoplasia [16].

The mechanism of action of IUD on its protection against cervical neoplasia is not yet fully established and it is still riddled with controversy. Xavier Castellsague and co-authors proposed that complete destruction of precancerous lesions by abrasion during IUD insertion could be an explanation for the effect [14]. However, Karl Ulrich Petry and co-authors disagreed with Castellsague et al., and proposed that the tissue trauma associated with IUD insertion induced a cellular immune response that might finally clear persistent HPV infections and pre-invasive lesions [17,18].

The uptake of modern contraception of 10% [19], in Nigeria is very poor. This controversy on association between IUD and cervical neoplasia may further hamper the poor uptake of modern contraception. There has been paucity of studies in this subject in sub-Saharan Africa. It is because of this, the study on association between IUD and cervical neoplasia was embarked upon. This study was aimed at evaluating the association between IUD and cervical neoplasia.

MATERIALS AND METHODS

This case-control study was carried out at the cervical cancer screening unit of the University of Nigeria Teaching Hospital (UNTH), Enugu between October 1, 2012 and December 31, 2013. Women (n=156) using Copper T 380A intrauterine contraceptive device were recruited from the Family Planning Clinic of UNTH. Women (n=156) who were not on any form of modern contraception (condoms, pills, injectables, IUDs, implants, and female or male sterilization) were recruited from the General Out-patient Department and Gynecology Clinic of UNTH constituted the control group.

Sampling technique involved a systematic random sampling, in which every 3rd client in the attendance register of each of the afore-mentioned clinics was picked after an initial random start. Individual counseling was done while the consenting participants were recruited for the study. All participants had Pap smear cytology. The participants with abnormal cervical smear cytology results and inflammatory lesions further had colposcopy. Biopsy specimen for histology was collected from the participants with suspicious lesions under colposcopy. The participants in the 2 groups were matched for age, parity and marital status. The age matching was used in a 5 year age grouping - 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40-44 years and 45-49 years. The matching for parity was also grouped into nulliparity, primiparity, multiparity and grand-multiparity. A structured questionnaire was used to collect bio-demographic information from all the participants. However pregnant women, women who declined consent despite adequate counselling, those who were taking alcohol and or tobacco, and women on IUD for less than one year were excluded from the study. There was no case of withdrawal or re-insertion among the study participants.

A minimum sample size for each of the 2 groups was calculated using the Formula [20]: $N = Z^2 (P) (1 – P)/d^2$ where, N = minimum sample size at 95% confidence level; Z = the standard normal deviate usually set at 1.96; d = precision: the difference between the true population rate and acceptable sample rate and it was set at 0.05; P = population prevalence from previous study and 7.3% [21], was used as the prevalence of abnormal cervical cytology of women currently using IUD in Turkey. 'N' was calculated thus: 1.96 x 1.96 x 0.073 x (1-0.073)/0.05x0.05=104. Adding 20% attrition rate, the minimal sample size of each of the 2 groups was 125.

STATISTICAL ANALYSIS

The data was analysed using the Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS IBM Corporation, Armonk, NY, USA). Mc Nemar Chi- square for matched pair studies was used to analyse the categorical data while t-test was used for continuous variables. All statistical analyses were at the 95% confidence interval. The p-value ≤ 0.05 was considered statistically significant. Ethical clearance for the study was obtained from the ethics committee of UNTH, Enugu.

RESULTS

A total of 312 women who met the inclusion criteria participated in the study. One hundred and fifty six women were categorized into each of the 2 groups. The age distribution of the participants showed that they were between 20 and 49 years with their mean age of 37.56±7.87 years. The mean duration of use of IUD by the participants using IUD was 42.32±11.32 months [Table/Fig-1] compares the socio-demographic variables between the participants using IUD and non-users of modern contraception. There was no statistical significant difference between the 2 groups of participants on these variables.

[Table/Fig-2] summarizes the Pap smear cytology results between participants using IUD and non-users of modern contraception. There was no statistical significant difference on abnormal cervical

Demographic data	Participants using IUCD (N=156) Frequency (%)	Participants on no modern contraception (N=156) Frequency(%)	p-value
Age (Years)			
20-24	9	9	0.95*
25-29	23	23	0.95*
30-34	19	19	0.95*
35-39	35	35	0.95*
40-44	36	36	0.95*
45-49	34	34	0.95*
Parity			
0	7	7	0.95*
1	24	24	0.95*
2-4	63	63	0.95*
>4	62	62	0.95*
Marital status			
Married	130	130	0.95*
Unmarried	26	26	0.95*
Occupation			
Unemployed	32(20.5)	30(19.4)	0.86
Teaching	8(5.1)	10(6.5)	0.87
Civil service	58(37.2)	50(32.3)	0.40
Trading	33(21.2)	40(25.8)	0.46
Artisans	10(6.4)	15(9.7)	0.61
Professionals	15(9.6)	10(6.5)	0.61
Education			
No formal	2(1.3)	1(0.65)	0.95
Primary	23(14.7)	15(9.7)	0.40
Secondary	31(19.9)	44(28.4)	0.16
Tertiary	100(64.1)	95(61.3)	0.61
Address			
Rural	41(30.8)	36(23.1)	0.61
Urban	115(69.2)	120(76.9)	0.61
Mean age of coitarche	18.83±2.56 years	19.20±2.81 years	0.23

[Table/Fig-1]: Comparison of socio-demographic characteristics between the women using IUD and non-users of modern contraception in Enugu, Nigeria.
*=Matched criteria

Pap smear result	N=156 Frequency	Percentage
Participants using IUD		
Negative to Squamous Intraepithelial Lesion	140	89.7
Atypical squamous cell of undetermined significance	6	3.8
Low grade squamous intraepithelial lesion	7	4.5
High grade squamous intraepithelial lesion	3	1.9
Participants on no form of modern contraception		
Negative to Squamous Intraepithelial Lesion	146	93.6
Atypical squamous cell of undetermined significance	2	1.3
Low grade squamous intraepithelial lesion	6	3.8
High grade squamous intraepithelial lesion	2	1.3

[Table/Fig-2]: Pap smear cytology results of the participants and mean duration of use of IUD by participants using IUD.
Note: Totals of 9 (6.4%) and 6 (4.1%) negative to squamous intraepithelial lesions among the participants on IUD and those on no form of modern contraception, respectively, were inflammatory cells. Comparison of cervical epithelial abnormalities between the 2 groups of women (16 versus 10; p-value= 0.53)

Colposcopy results	Participants using IUD (N=25) Frequency (%)	Participants on no form of modern contraception (N=16) Frequency (%)	p-value
Normal lesions	10(40)	4(25)	0.75
Suspicious lesions	15(60)	12(75)	

[Table/Fig-3]: Comparison of colposcopy results of abnormal pap smear between participants using IUD and those on no form of modern contraception.

cytology between the participants using IUD and non-users of modern contraception (16 versus 10; p-value=0.53). [Table/Fig-3] compares the colposcopy results of the participants using IUD and non-users of modern contraception. There was no statistical significant difference between them on colposcopy finding of suspicious lesions. [Table/Fig-4] also compares the histology results of the biopsy specimens of suspicious colposcopy lesions between participants using IUD and those on no form of modern contraception. There was no statistical significant difference between them on cervical neoplasia.

Histology results	Participants using IUD (N=15) Frequency (%)	Participants on no form of modern contraception (N=12) Frequency (%)	p-value
Normal	2(13.3)	3(25)	0.44
Inflammation	4(26.7)	3(25)	0.72
CIN 1	7(46.7)	5(41.6)	1.00
CIN 2	2(13.3)	1(8.3)	1.00

[Table/Fig-4]: Comparison of histology results of biopsy specimens of suspicious colposcopy lesions between participants using IUD and those on no form of modern contraception.
The comparison of cervical neoplasia between the participants using IUD and non-users of modern contraception (9 versus 6; p-value=0.78)

DISCUSSION

The prevalence of abnormal cervical cytology of 10.3%(16/156) reported among the IUD users in this study was similar to 7.3%(25/343) reported among IUD users in Turkey [18]. More so, the prevalence of cervical neoplasia of 5.8%(9/156) reported among the IUD users in this study was similar to 4% prevalence which was initially reported in Malaysia [9]. The overall prevalence of cervical neoplasia of 4.8%(15/312) reported in this study was slightly higher than 3.06% previously reported in Egypt [22]. However, it was similar to 4.8% reported in Zaria but less than 9.1% reported in Ibadan [23,24]. In this study, the overall CIN 1 and CIN 2 accounting for 3.9% (12/312) and 0.9%(3/312) respectively was similar to the findings in Zaria [23]. As was previously reported in India [2], none of the cases among IUD users in this study had malignant transformation. The absence of statistical significant difference between the participants using IUD and non-users of modern contraception in this study is supported by the previous reports in USA, Israel, the New Zealand and other centres [6,7,12,13]. However, this was contrary to the reports in India, Wales and Malaysia [2,3,9,10].

The non-existence of statistical significant difference on cervical inflammatory changes between the women using IUD and non-users of modern contraception was contrary to the report in Egypt which showed that cervical inflammatory changes were more associated with women who were using IUD than others [22].

LIMITATION

This study is weakened by its hospital-based design in which its finding may not be a true reflection of what is happening in the society. It is also limited by its cross-sectional pattern in which some of the information sought from the study participants were prone to recall bias.

CONCLUSION

Even though the proportion of women who had CIN was more among women using IUD than non-users of modern contraception, their difference in cervical neoplasia in this study was not statistically significant. Therefore, there was no significant association between IUD and cervical neoplasia in this study. This implies that IUD use by the family planning providers on clients who require it might be safe. There is need to conduct a randomised controlled study on this subject matter in this environment to further strengthen or refute the safety of IUD use as well as ascertain its protective effect.

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