ORIGINAL ARTICLE

Association Between Hormonal Contraceptives and Cervical Neoplasia in **Local Population of Khyber Pakhtunkhwa**

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ABSTRACT

Background: Hormonal contraception and the risk of developing cervical cancer is a contentious topic. These debates may reduce the popularity of hormonal birth control.

Objectives: The goal of this study is to assess the prevalence of Cervical Smear abnormalities among Peshawar's multiethnic population in relation to the usage of hormonal contraceptives.

Methods: This was a Case Control Study conducted on the females visiting DHQ Teaching Hospital Swabi, RHSC (A) KTH, HMC, LRH and FWC's in district Peshawar who were persistent long-term users for more than 5 years of any type of hormonal contraception. The study was conducted during the period from 1st August, 2021 to 30th January, 2022. We made two groups, one who had never used any method of contraception and the other persistent users of hormonal contraception. After approval from ethical committee and an informed consent of the client, enrollment in the study was made.

Results: A total of 300 patients were included in this study. 150 were cases whereas 150 were controls. Mean and SDs For Age 30+4.6 28+4.92. In the hormonal group, for type of contraceptives used, 98 (65.33%) patients used injectable, 40 (26.66%) patients used OCP whereas 12 (8%) patients used implants. As per frequencies and percentages for duration of use of contraceptives in the hormonal group, 120 (80%) were using different types of contraceptives for less than or equal to seven years whereas 30 (20%) were found using contraceptives for more than seven years As per frequencies and percentages for smear results in both groups, only 3 (2%) patients were found having atypical smear results who using injectable contraceptives for more than seven years however in the control group only 02 (1.33%) patient were having atypical smear results.

Conclusion: Our research did not identify any correlation between using birth control and having an abnormal Pap smear. Additional prospective research is needed.

Keywords: Pap smear, Abnormal, and Oral Contraceptive Pill (OCP).

INTRODUCTION

Cervical cancer ranks second in frequency among female cancers in low- and middle-income nations [1]. The most significant cause of cervical cancer is thought to be the persistent infection of cervical epithelial cells with particular high-risk forms of human papillomavirus (HPV) [2,3]. There is strong evidence that a large percentage of sexually active women acquire infections with HPV (16, 18), the kinds of HPV most strongly linked to cervical cancer.

Long-term usage of hormonal contraceptives is associated with an increased risk of persistent HPV infection and cervical cancer in HPV-infected women. You can get your hands on hormonal contraceptives in many different delivery systems, including COCP, POP, implants, IUDs, and injectables. In our country, COCPS and injectables are the two most popular options. The chance of developing cervical cancer increases after five years or more of oral contraceptive use [4]. The death rate from cervical cancer in the industrialized world has decreased by more than 70 percent thanks to the widespread use of the Pap smear as a screening test that can detect dyskaryosis with great sensitivity.

More than double the risk of developing cervical cancer, according to a meta-analysis of 24 epidemiological studies involving over 1.3 million women. Risk tends to decrease with time for women who have stopped using oral contraceptives, regardless of how long they were using them [5].

Using data from 8 studies, the International Agency for Research on Cancer (IARC), part of the World Health Organization, published a report in 2002 assessing the connection between OCPs usage and Ca Cervix Risk among users who had used OCPs continuously for 5-9 years compared with non-users. When compared to women who did not take OCPs, the chance of developing Ca Cervix was 4 times higher among women who used them for 10 years or more [6]. Hormones in OCPs could alter cervical cell susceptibility to HPV infection, alter the cells' ability to clear infection, or make it simpler for HPV infection to trigger alterations that proceed to cervical cancer [7].

The cumulative incidence of CIN by age 50 in less developed nations increased from 7.3 to 8.3 per 1000 in one research of current users of OCPs who had taken the product for more than 10 years, starting in their 20s or 30s [8]. The odds ratio (OR) for OCP and Ca Cervix use was 2.82 for 5-9 years and 4.03 for 10 years or more, according to a separate study [9].

Similarly, we are investigating the impact of long-term usage of hormonal contraceptives on pap smears in the district of Peshawar at three main RHSC (A) centers (KTH, HMC, and LRH). An early detection of cervical smear changes in clients of family planning services is an important goal, and this baseline study would pave the way for future cohort studies to accomplish this. Planners for people with disabilities in Pakistan could use this information to better decide how to deliver secure, high-quality family planning services [10].

MATERIALS AND METHODS

This was a Case Control Study conducted the females visiting DHQ Teaching Hospital Swabi, RHSC (A) KTH, HMC, LRH and FWC's in district Peshawar who were persistent long-term users for more than 5 years of any type of hormonal contraception. We carried out this study during the period from 1st August, 2021 to 30th January, 2022. We were including all clients eligible as per Medical Eligibility Criteria (MEC). It might extend to 300 clients in total. 150 in each group (Cases and Control) All case were selected through non probability consecutive sampling using the following selection criteria, sexually active women of age b/w 20-45 years and persistent users for last 5 years. Women not eligible as per MEC were excluded from the study. We made two groups, one who had never used any method of contraception and the other persistent users of hormonal contraception. After approval from ethical committee and an informed consent of the client, enrollment in the study was made. We performed Pap smear in RHSCA. The smear was sent to the pathology department of the hospital for cytology and reporting. Results were documented and the clients were informed of the result status. The data was then interpreted taking into account the age, Parity, duration of use, any co existent STI and the result of Pap smear. In Case of abnormal result, guided as per protocols for HPV and Coloposcopy and a referral was done with proper liaison with Gynae Department.

Statistical analysis and data entry were performed using SPSS version 20. Numberal variables, such as age and length of time on contraceptives, were used to compute means and standard deviations. Frequencies and percentages were calculated for categorical variables like number of children's, education level and income level. All the result was presented in the form of tables or graphs.

RESULTS

Research was done at the Obstetrics and Gynecology clinics of Lady Reaching Hospital, Khyber Teaching Hospital, and Hayatabad Medical Complex in Peshawar. One hundred and fifty people were enrolled in the study. Cases numbered 150, and controls numbered 150. Mean and SDs For Age 30+4.6

28+4.92. As per frequencies and percentages for age wise distribution, 93 (62%) patients in 20-30 years age group were controls and 57 (28%) patients in 31-45 age groups were also controls. In the same manner, 93 (62%) patients in 20-30 years age group were cases and 57 (28%) patients in 31-45 age groups were also cases. (Table No. 1).

As per no of children in both groups, 78 (42%) patients in controls were having children less than or equal to two in number whereas 72 (48%) were having children greater than two in number. Similarly, in our cases, 59 (39.33%) patients were having children less than or equal to two in number whereas 91 (60.66%) in cases were having children greater than two in number. (Table No. 2).

Keeping in view the education level in both groups, 18 (12%) patients were found uneducated, 86 (57.33%) patients were found having primary education, 29 (19.33%) patients having secondary education and only 17 (11.33%) patients were having higher education in all the controls. In the same manner, in cases group, 59 (39.33%) were found uneducated, 34 (22.66%) were having primary education, 50 (33.33%) were having secondary education whereas only 07 (4.66%) patients had higher education. (Table No. 3)

As per income status, in controls, 74 (49.33%) patients were having income less than or equal to Rs 35,000/- per month whereas in the same group, 76 (50.66%) patients were having income status above Rs 35,000/- per month. In cases, 65 (43.33%) patients were having income less than or equal to Rs 35,000/- per month whereas in the same group, 85 (56.66%) patients were having income above 35,000/- per month. (Table No. 4)

In the hormonal group, for type of contraceptives used, 98 (65.33%) patients used injectable, 40 (26.66%) patients used OCP whereas 12 (8%) patients used implants. (Table No. 5).

As per frequencies and percentages for duration of use of contraceptives in the hormonal group, 120 (80%) were using different types of contraceptives for less than or equal to seven years whereas 30 (20%) were found using contraceptives for more than seven years. (Table No. 6).

As per frequencies and percentages for smear results in both groups, only 3 (2%) patients were found having atypical smear results who using injectable contraceptives for more than seven years however in the control group only 02 (1.33%) patient were having atypical smear results. This shows that long term usage of contraceptive increases the risk of having Cervical Smear abnormalities. (Table No. 6).

Table 1: Age distribution (n=300)

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Age group	Controls	Cases
20-30 Years	93 (62%)	93 (62%)
31-45 Years	57 (28%)	57 (28%)
Mean and SDs For Age	30+4.6	28+4.92

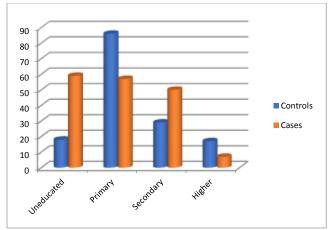


Fig.1: Age distribution graph

Table.2: frequencies and percentage of income status (n=30)

Income status	Controls	Cases
< Rs 35000 per month	74 (49.33%)	65 (43.33%)
> Rs 35000 per month	76 (50.66%)	85 (56.66%)

Table 3: frequency and percentage for contraceptive used in hormonal group (n=150)

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	Type of contraceptives used	Frequencies	Percentages
	Injectables	98	65.33%
	OCP	40	26.66%
	Implants	12	8%

Table 4: frequency and percentage for contraceptive used in hormonal group (n=150)

Duration of use	Frequencies	Percentages
< 7 Years	120	80%
> 7 Years	30	20%

Table 5: frequency and percentage for smear results in both group (n=150

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Smear results	Controls	Cases	
Normal	148 (98.66%)	147 (98%)	
Atypical	02 (1.33%)	03 (2%)	

Table 6: stratification of smear results with age (n=150)

Age	Smear	Controls	Cases	P Value
	Results			
20-30 Years	Normal	90 (60%)	91 (60.66%)	
	Atypical	01 (0.66%)	02 (1.33%)	0.573
31-45 Years	Normal	58 (38.66%)	56 (37.33%)	
	Atypical	01 (0.66%)	01 (0.66%)	0.980

DISCUSSION

Cervical cancer ranks second in frequency among female cancers in low- and middle-income nations [11]. The most significant cause of cervical cancer is thought to be the persistent infection of cervical epithelial cells with particular high-risk forms of human papillomavirus (HPV) (2,3). There is strong evidence that a large percentage of sexually active women acquire infections with HPV (16, 18), the kinds of HPV most strongly linked to cervical cancer [12].

Long-term usage of hormonal contraceptives is associated with an increased risk of persistent HPV infection and cervical cancer in HPV-infected women. You can get your hands on hormonal contraceptives in many different delivery systems, including COCP, POP, implants, IUDs, and injectables. In our country, COCPS and injectables are the two most popular options. The chance of developing cervical cancer increases after five years or more of oral contraceptive use [13]. The death rate from cervical cancer in the industrialized world has decreased by more than 70 percent thanks to the widespread use of the Pap smear as a screening test that can detect dyskaryosis with great sensitivity.

More than double the risk of developing cervical cancer, according to a meta-analysis of 24 epidemiological studies involving over 1.3 million women. Risk tends to decrease with time for women who have stopped using oral contraceptives, regardless of how long they were using them [14]. Based on the study's frequency and percentage analysis of smear findings, we observed that only 3% of patients using injectable contraceptives for more than 7 years had atypical smear results, whereas only 1.3% of patients in the control group did as well. This demonstrates that there is an association between long-term contraceptive use and Cervical Smear abnormalities. Seventh Table.

Using data from 8 studies, the International Agency for Research on Cancer (IARC), part of the World Health Organization, published a report in 2002 assessing the connection between OCPs usage and Ca Cervix Risk among users who had used OCPs continuously for 5-9 years compared with non-users. Compared to my study, which looked at women who had used oral contraceptives for at least 10 years, the risk of Ca Cervix was four times as high among women who had used OCPs for at least 10 years (60). However, according to the frequencies and percentages for smear results in both groups, only three patients using injectable contraceptives for more than seven years were found to have atypical smear results. Long-term contraceptive use is associated with an elevated incidence of Cervical Smear abnormalities, as seen here. Referring to Table No. 7. OCPs contain hormones that may increase cervical cell vulnerability to HPV infection, impair their capacity to clear infection, or make it simpler for HPV infection to initiate alterations that lead to cervical cancer [15]. Compared to my study, which found that only 3% of patients using injectable contraceptives had atypical smear results, one study found that current users of OCPs using it for more than 10 years, using it from around age 20-30 years, increase the cumulative incidence of CIN by the age 50 from 7.3 to 8.3 per 1000 in less developed countries [16]. This demonstrates that there is a correlation between prolonged contraceptive use and Cervical Smear abnormalities. As shown in Table No. 6.

According to the frequencies and percentages for smear results in both groups, only 3 (2 percent) patients were found having atypical smear results who were using injectable contraceptives for more than seven years, while in the control group, only 02 (1.33 percent) patient were having atypical smear results [17]. This demonstrates that there is a correlation between prolonged contraceptive use and Cervical Smear abnormalities [18]. As shown in Table No. 6.

CONCLUSION

Our research did not identify any correlation between using birth control and having an abnormal Pap smear. Additional prospective research is needed.

REFERENCES

 Tang, M. J., Ding, S. B., & Hu, W. Y. (2019). Fibrinogen and albumin score changes during preoperative treatment can predict prognosis in

- patients with locally advanced rectal cancer. Gastroenterology research and practice, 2019.
- Choi, H. (2019). Can quadrivalent human papillomavirus prophylactic vaccine be an effective alternative for the therapeutic management of genital warts? An exploratory study. International braz j urol, 45, 361-368
- Rahaman, H. A., Chinnikatti, S. K., Al Miraj, A. K., Rahman, M. M., & Khan, M. S. U. (2020). Scholars Journal of Applied Medical Sciences.
- Sui, S., Jiao, Z., Chen, H., Niyazi, M., & Wang, L. (2020). Association between APOBEC3s and HPV16 E2 gene hypermutation in Uygur females with cervical cancer. Oncology Letters, 20(2), 1752-1760.
- Nguyen, D. N. T., Simms, K., Nguyen, H. Q. V., Van Tran, T., Nguyen, N. H., LaMontagne, D. S., ... & Canfell, K. (2019). The burden of cervical cancer in Vietnam: synthesis of the evidence. Cancer epidemiology, 59, 83-103.
- Tomita, L. Y., Horta, B. L., da Silva, L. L. S., Malta, M. B., Franco, E. L., & Cardoso, M. A. (2021). Fruits and vegetables and cervical cancer: A systematic review and meta-analysis. Nutrition and Cancer, 73(1), 62-74.
- Samanta, M., & Maiti, M. (2022). Effects of oral contraceptive pill on female health. Int. J. Exp. Res. Rev, 28, 15-24.
- Osman, S. E., Elmadenah, E. M., Elmahi, O. M., Alkarsani, M. E., Eltayeb, L. B., & Waggiallah, H. A. Cytomorphometric Analysis of Cervical Papanicolaou Smear for Females with Gynecological Clinical Complaints
- Baik, S., Mehta, F. F., Unsal, E., Park, Y., & Chung, S. H. (2022).
 Estrogen Inhibits Epithelial Progesterone Receptor-Dependent Progestin Therapy Efficacy in a Mouse Model of Cervical Cancer. The American Journal of Pathology, 192(2), 353-360.
- Dorji, T., Pokhrel, H. P., & Tshokey, T. (2020). Socio-demographic and clinical characteristic of women availing pap smear services in Samtse District, Bhutan. Asian Pacific Journal of Cancer Biology, 5(2), 63-70.
- Arend, D. L. (2021). Evaluating the Impact of the ACOG HPV Vaccination Toolkit on Vaccination Rates (Doctoral dissertation, Grand Canyon University).
- Reed, A. (2022). COVID: A Silver Linings Playbook: Mobilizing Pandemic Era Success Stories to Advance Reproductive Justice. Berkeley J. Gender L. & Just., 37, 221.
- Menon, S. (2018). Cervical cancer prevention in HIV-infected women within a high bacterial vaginosis setting in Kenya (Doctoral dissertation, Ghent University).
- Delston, J. B. (2019). Medical Sexism: Contraception Access, Reproductive Medicine, and Health Care. Lexington Books.
- Kraetschmer, K. (2022). The Contraceptive Methods Table as Preventive Instrument for Avoiding Abortion. Am J Obstetr Gynecol Res, 2(1), 1008.
- Henderson, J., & Henderson, P. (2021). "Don't Necessarily" Trust Me, I'm a Doctor: A Roadmap to finding a trustworthy health care provider and avoiding the dangers of not doing so. Gatekeeper Press.
- Martin-Plank, L. (2018). Urological and Gynecological Disorders. Advanced Practice Nursing in the Care of Older Adults, 280
- Bruce, L. (2020, June). A pot ignored boils on: sustained calls for explicit consent of intimate medical exams. In Hec Forum (Vol. 32, No. 2, pp. 125-145). Springer Netherlands.