

## CORRELATION OF THE USE OF CONTRACEPTIVE PILL COMBINATION TO RISK OF LEIOMYOMA EVENTS IN RSPAL SURABAYA

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### ABSTRACT

**Introduction:** *The use of contraception is important to control population growth, regulate the interval between pregnancies, avoid unwanted births, control the time of birth in a husband and wife relationship and determine the number of children in the family. According to the Central Statistics Agency (BPS) of East Java Province in 2018, the number of active Family Planning (KB) participants of married women of childbearing age who use hormonal contraception in the form of pills was 19.26%, injections were 50.44%, and implants is 11.45%. Uterine fibroids occur in 20%-25% of women of reproductive age. The prevalence of leiomyoma may increase with hormonal contraceptives containing the hormone estrogen, either pure or combined. Uterine fibroids can affect the quality of life of the sufferer.*

**Purpose:** *To analyze the relationship between the use of combined pill contraceptives and those who do not use the combined pill contraception in women with the incidence of leiomyoma.*

**Method:** *This research is an observational analytic carried out retrospectively with a case-control approach. The sampling technique in this study was non-probability sampling, namely purposive sampling. This study uses secondary data, namely medical records of gynecological patients at the RSPAL Dr. Ramelan Surabaya by meeting the inclusion criteria and exclusion criteria. The data collected will be analyzed by looking at whether leiomyoma patients use combined pill contraception.*

**Result:** *Patients diagnosed with leiomyoma who used the combined pill contraceptive were 48 (63%), while those who did not use the combined pill were 28 (37%). This study's results indicate a significant relationship between the use of combined pill contraceptives and the incidence of leiomyoma ( $p=0.001$ ).*

**Conclusion:** *There is a relationship between the use of combined pill contraceptives with the incidence of leiomyoma.*

**Keywords:** *leiomyoma, contraception, combination birth control pills*

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## INTRODUCTION

The use of contraception aims to control population growth, adjust the distance between pregnancies, prevent unwanted births, and regulate the number of children in a family.<sup>1</sup> According to the Central Statistics Agency (BPS) of East Java Province in 2018, the number of women of childbearing age who are married who use active family planning (KB) are as follows, who use hormonal contraception in the form of pills by 19.26%, injections by 50.44% and implants by 11.45%.<sup>2</sup> Contraceptive pill combinations are pills that use synthetic estrogen and progesterone as raw materials.

Leiomyoma occurs in 20%-25% of women of reproductive age.<sup>1</sup> Leiomyoma is rare in women aged 20 years and has never even been reported to appear in women who have not experienced menstruation.<sup>3</sup> Leiomyoma are often found in the 40-49 year age group with an average age of 42.97 years, as much as 51%.<sup>4</sup> The prevalence of uterine myomas in Surabaya was recorded at 10.03%, and in Riau, 8.03% of all gynecological patients were treated. According to data at the RSUP Prof. Dr. R.D. Kandou Manado, as many as 408 cases of leiomyoma were found in 2011-2013, with details of 112 cases (16%) in 2011, 168 cases (25%) in 2012, and 128 cases (25.6%) in 2013.<sup>5</sup> Leiomyoma can affect the quality of life of the sufferer. In addition, leiomyoma is also one of the comorbidities in infertile women. Symptoms of leiomyoma can affect the daily physical activities of women of childbearing age. Daily activities can be disrupted by symptoms such as vaginal bleeding, metrorrhagia, pain, and menorrhagia.<sup>6</sup> The purpose of this study was to analyze the relationship between the use of combined pill contraceptives and those who did not use the combined pill contraception in women with the incidence of leiomyoma. This study was conducted on women aged 35-50, diagnosed with uterine fibroids, and using combined hormonal contraceptive pills for more than five years.<sup>7</sup>

## METHOD

This study used an observational analytic design that was carried out retrospectively with a case-control approach to see the relationship between combined pill contraceptive use (independent variable) and the incidence of leiomyoma (dependent variable) at the Rumah Sakit Pusat Angkatan Laut Dr. Ramelan Surabaya. The sampling technique in this study was a non-probability sampling method, namely purposive sampling. In this purposive sampling, the researcher chooses based on subjective considerations and the inclusion and exclusion criteria that have been determined. In this study, the total number of respondents was 152 gynecological patients consisting of 76 gynecological patients with a diagnosis of leiomyoma with inclusion and exclusion criteria and 76 gynecological patients without a diagnosis of leiomyoma with inclusion and exclusion criteria.

The inclusion criteria in this study were complete medical records of female patients aged 35-50 years with gynecological examination data and contraceptive use recorded in the medical record from May 1, 2019, to May 31, 2021. And for the exclusion criteria are women who are pregnant, women who are already menopause, and women with other gynecological diseases, including abnormal uterine bleeding, endometriosis, inflammation and infection of the genitals, injuries to the genitals, benign vulvar tumors, benign vaginal tumors, benign cervical benign tumor, benign endometrial tumor, adenomyosis, benign ovarian tissue tumor, ovarian epithelial tumor, benign uterine tube tumor, and malignant genital organ tumor, and body mass index  $\geq 23$  kg/m<sup>2</sup>.

Researchers used the Chi-Square test as a data analysis technique to determine the relationship between the independent and dependent variables. Data analysis was performed using SPSS software on a computer.

## RESULTS

This study used bivariate analysis to determine the relationship between the two variables studied: combined pill contraception (independent variable) and leiomyoma (dependent variable). This study uses secondary data, which is complete medical records of female patients aged 35-50 years with gynecological examination data and contraceptive use

recorded in medical records from May 1, 2019, to May 31, 2021, at the Rumah Sakit Pusat Angkatan Laut Dr. Ramelan Surabaya by meeting the inclusion criteria and exclusion criteria as well as interviews with patients by asking about the history of using the combined pill contraception which was previously preceded by giving informed consent. Then the data analysis was carried out; the following results were obtained:

**Table 1. Characteristics of leiomyoma patients at the Rumah Sakit Pusat Angkatan Laut Dr. Ramelan Surabaya by age.**

Variable	Case group		Control group	
	n	Percentage (%)	n	Percentage (%)
<i>Ages<sup>8</sup></i>				
Early adulthood (26-35)	0	0	8	10,5
Late adult (36-45)	42	55,3	44	57,9
Early elderly (46-55)	34	44,7	24	31,6
<b>Total</b>	<b>76</b>	<b>100</b>	<b>76</b>	<b>100</b>

Table 1 shows that the subjects were 76 women with early adulthood (26-35 years) amounted to 0 people (0%), late adults (36-

45 years) amounted to 42 people (55.3%), and the elderly initial (46-55 years) amounted to 34 people (44.7%).

**Table 2. According to the history of contraceptive pill combination use, the characteristics of leiomyoma patients at the Rumah Sakit Pusat Angkatan Laut Dr. Ramelan Surabaya.**

Variable	Case group		Control group	
	n	Percentage (%)	n	Percentage (%)
<i>The use of contraceptive pill combination</i>				
Used	48	63,2	27	35,5
Never used	28	36,8	49	64,5
<b>Total</b>	<b>76</b>	<b>100</b>	<b>76</b>	<b>100</b>

Table 2, based on the history of contraceptive pill combination use, 48 people (63.2%) used combined pill

contraception, and 28 people (36.8%) did not use combined pill contraception.

**Table 3. Analysis of the Relationship between contraceptive pill combination use and leiomyoma incidence.**

<i>The use of contraceptive pill combination</i>	<i>Leiomyoma</i>				<i>Total</i>	<i>P-value</i>
	<i>Diagnosed</i>		<i>Undiagnosed</i>			
	<i>n = 76</i>	<i>%</i>	<i>n = 76</i>	<i>%</i>		
<i>Used</i>	48	63,2	27	35,5	75	0,001
<i>Never used</i>	28	36,8	49	64,5	77	
<i>Total</i>	76	100	76	100	152	

Table 3 shows that 48 patients (63.2%) were diagnosed with leiomyoma using the contraceptive pill combination, while 28 patients (36.8%). Twenty-seven patients (35.5%), undiagnosed leiomyoma and using contraceptive pill combination (64.5%).

Based on the data analysis of the relationship between the use of contraceptive pill combination and the incidence of leiomyoma, data analysis was carried out using SPSS with Chi-Square test to determine the relationship between independent and dependent variables with nominal data scale, obtained p-value = 0.001 which means there is a significant relationship between the use of contraceptive pill combination with the incidence of leiomyoma so that there is a difference in the proportion of leiomyomas with the use of contraceptive pill combination.

## DISCUSSION

Genetic mutations can increase the production of estrogen receptors; as compensation, estrogen levels increase due to high aromatase activation, thereby increasing cell proliferation by inhibiting the apoptotic pathway and stimulating the production of cytokines and PDGF and EGF. In addition, estrogen also stimulates the formation of progesterone receptors so

that through stimulation of IGF-1, TGF and EGF can form tumors.

Myoma uteri will create a hyperestrogenic environment for the growth and maintenance of leiomyoma. Leiomyoma cells contain more estrogen receptors which produce more estradiol binding. These tumors convert less estradiol to weaker estrone. The use of contraceptive pill combinations can also contribute to a large number of estradiol bonds due to its content, namely the ethynyl group at the C 17 atom. If eaten per os, its efficacy will increase because these substances are not easily changed through the portal system.

Progesterone is considered an important mitogen in the growth and development of leiomyoma. Therefore, cell proliferation, extracellular matrix accumulation, and cell hypertrophy are controlled by progesterone directly and in a permissive role by estrogen. According to Eric J. Bieber, most studies show that leiomyoma has higher estrogen concentrations than normal myometrium. Upregulation of ESR2 in leiomyoma is very significant because of the participation of chromosome 14 and the finding of translocations of chromosomes 12, 14 in uterine myomas.<sup>7</sup> This study follows previous research conducted by Tumaji and colleagues (2020) regarding the effect of reproductive health history on the

incidence of leiomyoma in women in urban Indonesia, namely that there is a significant relationship between the use of contraceptive pill combination and the incidence of leiomyoma so that there is a difference in the proportion of leiomyoma with the use of contraceptive pill combination ( $p=0.001$ ).<sup>6</sup> The results of research conducted by Erlindawati and colleagues on the factors associated with the incidence of leiomyoma at the Bengkulu city hospital in 2012 concluded that the use of oral contraceptives that have a role in the growth of leiomyoma depends on the composition of estrogen and the type of progesterone in oral contraceptives such as the use of ethidodral diacetate progesterone preparations has been reported to increase the incidence of leiomyoma.<sup>9</sup> Research conducted by Jun Ying found that women who use oral contraceptives have a 1.91 times risk of developing leiomyoma than women who do not use oral contraceptives.<sup>10</sup>

## CONCLUSION

The results of the research conducted by the author are:

1. There is a relationship between the use of contraceptive pill combinations with the incidence of leiomyoma.
2. There is no relationship between the use of contraceptive pill combination with the incidence of leiomyoma.
3. There is a difference in the incidence of leiomyoma in women who use contraceptive pill combinations and those who do not use contraceptive pill combinations.

The conclusion of this study is those female patients who use contraceptive pill combinations have risk factors for the incidence of leiomyoma.

## ACKNOWLEDGEMENT

The author would like to thank the Chancellor of the Widya Mandala Catholic University, the Dean of the Faculty of

Medicine, Widya Mandala Catholic University, the two lecturers and examiners, all the Widya Mandala Catholic University Faculty of Medicine staff, all the RSAL Dr. Ramelan Surabaya staff, and the patients who were willing to be respondent.

## REFERENCES

1. Liwang F, Bhargah A, Kusuma IBH, Prathiwinda GG, Indaya IG, Putra S, et al. Gambaran penggunaan kontrasepsi hormonal dan non hormonal di wilayah kerja UPT Puskesmas Tampak Siring 1. *Fak Kedokt Univ Sam Ratulangi*. 2018;9(3):41–6.
2. Timur BK dan KBNPJ. Jumlah Pasangan Usia Subur dan Peserta KB Aktif di Provinsi Jawa Timur Menurut Kabupaten/Kota, 2018 [Internet]. Surabaya: Badan Pusat Statistik Provinsi Jawa Timur; 2018. Available from: <https://jatim.bps.go.id/statictable/2019/10/09/1683/jumlah-pasangan-usia-subur-dan-peserta-kb-aktif-di-provinsi-jawatimur-menurut-kabupaten-kota-2018-.html>.
3. Murti, Naomi. Analisis Faktor Pemicu Perkembangan Mioma Uteri pada Wanita Dewasa Akhir. 2019.
4. Lilyani DI, Sudiati M, Basuki R. Hubungan Faktor Risiko dan Kejadian Mioma Uteri di Rumah Sakit Umum Daerah Tugurejo Semarang. *J Kedokt Muhammadiyah*. 2012;1(1):14–9.
5. Pasinggi S, Wagey F, Rarung M. Prevalensi Mioma Uteri Berdasarkan Umur Di Rsup Prof. Dr. R. D. Kandou Manado. *e-CliniC*. 2015;3(1).
6. Izza N. Kejadian Mioma Uteri Pada Perempuan Di Perkotaan Indonesia. 2020;89–98.
7. Bieber EJ, Sanfilippo JS. *Clinical Gynecology*. second edi. United Kingdom: Cambridge University Press; 2015.

8. Amin M Al, Juniati D. Klasifikasi Kelompok Umur Manusia Berdasarkan Analisis Dimensi Fraktal Box Counting Dari Citra Wajah Dengan Deteksi Tepi Canny. *J Ilm Mat* [Internet]. 2017;2(6):34. Available from: <https://media.neliti.com/media/publications/249455-none-23b6a822.pdf>
9. Sumiati S, Erlindawati. Faktor-Faktor Yang Berhubungan Dengan Mioma Uteri Di Rumah Sakit Kota Bengkulu Tahun 2012. *J Media Kesehat* [Internet]. 2012;vol 5, No(3):101–205. Available from: <http://jurnal.poltekkes-kemenkes-bengkulu.ac.id/index.php/jmk/article/view/191>.
10. Ying J, Nie D. The relationship between the use of oral contraceptives and the risk of uterine leiomyoma in women of child bearing age of Han Chinese. *Pharm Bioprocess*. 2018;6(2):48–52.