Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2018; 9(4); 395-400

doi: 10.25258/ijpqa.9.4.7

ISSN 0975 9506

Research Article

Premalignant and Malignant Changes in Symptomatic Endometrial Polyps in Women Aged 20-70 years

Susan Abed Zaidan^{1,*}, Alaa Abdulqader Abdulrazaq², Eaman Marouf Muhammed³

¹C.A.B.O.G., University of Anhar, Iraq

²Pathology department, College of Medicine, Ibn Sina University of Medical and pharmaceutical sciences, Baghdad, Iraq

³F.I.C.O.G., C.A.B.O.G. Ob/gyn department, Al-Yarmouk Teaching Hospital, Baghdad, Iraq

Received: 22nd Oct, 18; Revised: 11th Nov, 18, Accepted: 5rd Dec, 18; Available Online: 25th Dec, 2018

ABSTRACT

Background: endometrial polyps are localized over growth of endometrium including glandular and stromal tissue with prominent angiogenesis regulated by growth factors. Polyps occur in different age group and could be asymptomatic and discovered incidentally or it cause abnormal premenopausal and postmenopausal bleeding. Most endometrial polyps are benign but premalignant and malignant changes also occur frequently. Objective: this study was carried out to identify the age-group in which endomaterial polyps are encountered in routine surgical pathology practice, to document the agegroup in which these polyps underwent malignant changes and to identify the histological subtype of endometrial polyps according to age group. Patients and methods: This prospective study conducted to demonstrate the premalignant and malignant changes in symptomatic endometrial polyps in relation to patients age group ranging from 20-70 years with abnormal uterine bleeding examined in gynecology & obstetric department in Al-Ramadi and Al-Yarmouk Teaching Hospital during the period from January 2017 to May 2018. The endometrial samples were obtained either by D&C, hysteroscopy or the polyps were demonstrated after surgical hysterectomy. All endometrial samples were fixed in 10% formalin solution and sent to the private histopathology laboratory in Baghdad for histopathological diagnosis. Results: The total number of examined women were 150. The most common recorded age was 20-70 years, 74.6% were premenopausal and 25.4% of patients were post-menopausal at the time of diagnosis. Most of patients presented with symptomatic polyps in this study were in age group 41-50 years (36.6%) in which most of the polyps were benign, while premalignant and malignant changes were more common in women between 51-60 years. The final pathological diagnoses showed benign endometrial polyps (49.3%), (48.6%) were pre-malignant polyps and (2 %) were malignant polyps. From benign lesions secretary endometrium was the most common finding in 43 cases (58.1%), while simple endometrial hyperplasia without atypia was the most common finding in the pre-malignant group 40 cases (54.7%). The distribution of histopathological changes in each age group were significant with a P value equal to 0.02. Conclusion: all endometrial polyps in pre- and post-menopausal women should be removed and submitted for histopathological examination as some of them even though there are benign but could carry areas of cellular atypia or malignant transformation.

Keywords: endometrial polyps, malignant changes, uterine bleeding.

INTRODUCTION

Endometrial polyps are localized endometrial overgrowth consisting of endometrial glands, stroma and blood vessels⁽¹⁾It is thought that they arise because of oestrogen hypersensitivity in certain areas of the endometrium causing endometrial stromal growth, angiogenesis and insensitivity to progesterone and this is mediated by angiogenic growth factors(2). Furthermore, they do not undergo shedding during menstruation because oestrogen dependent inflammation could block apoptosis(2).Other studies attribute endometrial polyps formation to local immunological disturbance⁽³⁾ . They are common gynecological disorder that could be asymptomatic or abnormal uterine bleeding postmenopausal bleeding (1). Nowadays, they are seen more frequently because of wide use of ultrasound in gynecological practice with overall prevalence of 7.8 % ⁽⁴⁾ increasing to 12.1% among women aged 45-50 years without symptoms ⁽⁵⁾ but the prevalence is higher (24%) among women presented with abnormal uterine bleeding ⁽⁶⁾. Increasing age is the major factor increasing the risk of development of endometrial polyp ⁽⁷⁾. Transvaginal ultrasound imaging is used for diagnosis of endometrial polyp and its diagnostic performance can be increased by intrauterine saline injection ⁽⁸⁾ or Doppler flowmetry ⁽⁹⁾. Most endometrial polyps are benign and premalignant and malignant changes found in about 5% of the cases ⁽¹⁰⁾. Other studies showed that the risk of malignancy is as low as 1.5 % ⁽¹¹⁾. This risk increases with increase woman age ^(12,13), menopausal state ⁽¹³⁾ and increase size of the

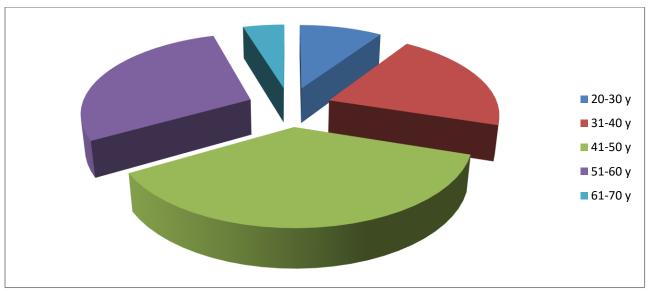


Figure 1: Frequency of endometrial polyp by age group.

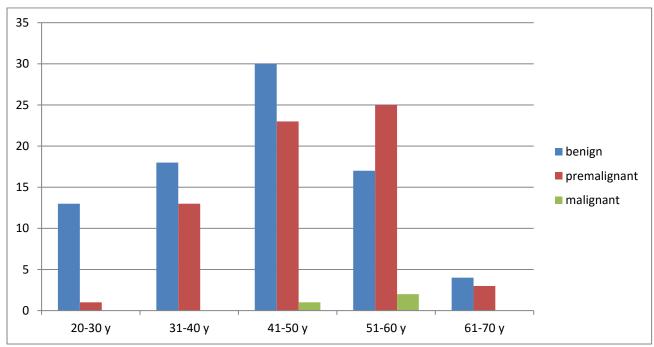


Figure 2: Distribution of benign, premalignant and malignant polyps by age group.

polyp ⁽¹⁴⁾. Also presence of abnormal vaginal bleeding has been identified as recognized factor increasing risk of malignancy within the polyp⁽¹⁵⁾. Hypertension, obesity and diabetes mellitus are also considered as risk factors for malignant transformation in endometrial polyp^(16,17) Regarding management of endometrial polyps, consensus guidelines are lacking. Medical treatment has limited role⁽¹⁾ and many studies advocate removal of all symptomatic polyp^(1,11,18,19) or those present in women with risk factors for malignancy⁽¹⁹⁾. On the other hand there is a study recommend removal of any endometrial polyp in pre- and postmenopausal women whether symptomatic or not⁽²⁰⁾. However, the women should be informed that growth pattern of polyp cannot accurately predicted ⁽⁶⁾. Hysteroscopic polypectomy is the most effective method of treatment ^(21,22). Blind removal is done

when hysteroscopically guided removal is not available $^{(1)}$. Both hysteroscopic and blind avulsion have low recurrence rate with minimal complications and technically feasible $^{(23)}$. Radical surgery in form of hysterectomy guarantees non recurrence and no malignant potential in the future but with greater morbidity and cost $^{(1)}$

MATERIAL & METHODS

This is a prospective study conducted to evaluate the premalignant and malignant changes in symptomatic endometrial polyps in relation to patients' age group ranging from 20-70 years with abnormal uterine bleeding examined in gynecology & obstetric department in Al-Ramadi and Al-Yarmouk Teaching Hospital / Baghdad-Iraq during the period from January 2017 to May 2018.

Table 1: No. of patient with endometrial polyps in each age group.

Age (years)	N=150	
Range	20-70	
Menopausal status:		
Pre-menopausal	112 (74.6%)	
Post-menopausal	38 (25.4%)	
20-30	14(9.3%)	
31-40	31(20.6%)	
41-50	55(36.6%)	
51-60	43(28.6%)	
61-70	7(4.6%)	

All affected females during the study period underwent removal of endometrial polyp (endometrial biopsy) either by D&C, hysteroscopy or the polyp demonstrated after surgical hysterectomy (as hysteroscopy not present in Al-Ramadi hospital so the samples were obtained by D&C or hysterectomy) . Endometrial samples were fixed in 10% formalin solution and sent to the private histopathology laboratory in Baghdad for processing and histopathological diagnosis.

Statistical analysis

Statistical analysis was performed using the Microsoft® Excel, Professional Edition 2010. Descriptive statistics (means and percentage) are mostly presented. Statistical significance was calculated using the ANOVA (Analysis of Variance) test . A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 150 histopathological specimens collected from women with symptomatic endometrial polyps were included in the study. The patients' mean age and standard deviation (SD) were 56.6±4 years, and range from 20-70 years. 74.6% were pre-menopausal at the time of diagnosis and 25.4% of patients were postmenopausal. The menopausal status and number of cases in each age group are illustrated in Table-1. The maximum number of patients presented symptomatic polyps in this study were in age group 41-50 years (36.6%), while the least were in the elderly group (4.6%) as shown in table-1 and figure-1. Figure-2 illustrates the number of benign, pre-malignant and malignant lesions as the underlying cause in different age groups. The number of benign polyps was highest in age group 41-50 years. Polyps with endometrial hyperplasia, the pre-malignant group, was highest in age group 51-60 years. This age group carried the highest number of malignant polyps also as shown in figure-2. The final

Table 2: The No. of cases according to the histopathological types of endometrial polyps (N=150)

	J F ~ (- · · - · · ·)
Variable	N(%)
Benign polyp	74(49.3%)
Marked secretary endometrial glands	43(28.6%)
Proliferative endometrial glands	17(11.3%)
Disordered proliferative endometrium	14(9.3%)
Premalignant polyp	73(48.6%)
Unclassified cystic glandular	13(8.6%)
hyperplasia	
Simple endometrial hyperplasia	40(26.6%)
without atypia	
Simple endometrial hyperplasia with	12(8%)
atypia	
Complex endometrial hyperplasia	2(1.3%)
without atypia	
Complex endometrial hyperplasia with	6(4%)
atypia	
Malignant polyp	3(2%)

pathological diagnoses showed 74 cases were benign endometrial polyps (49.3%), 73 cases (48.6%) were premalignant polyps and three cases only (2 %) were malignant polyps (Table-2). From benign lesions secretary endometrium was the most common finding in 43 cases (58.1% of benign lesions), while simple endometrial hyperplasia without atypia was the most common finding in the pre-malignant group 40 cases (54.7% of pre-malignant lesions). Table- 3 shows the histological types of polyps distributed in different age groups, the distribution of histopathological changes in each age group were significant with a P value equal to 0.02. Although polyps with endometrial hyperplasia, the pre-malignant group, was highest in age group 51-60 years, but the commonest subtype was simple endometrial hyperplasia with atypia and it's mostly seen in the 41-50 years age group as shown in figure-3. Different histopathological types of polyps were seen in the post-menopausal women. The most common type was endometrial hyperplasia without atypia as illustrates in figure-4

DISCUSSION

Endometrial polyps are commonly seen bothersome lesions. Polypectomy is usually done to treat the abnormal uterine bleeding and to detect possible premalignant or malignant endometrial changes. In agreement with the study conducted by Kanthi et al ⁽²³⁾, our study showed that rate of occurrence of endometrial

Table 3: Histological types of polyps according to age groups

Age	No.	Secretary	proliferative	Unclassified	Simple	Simple	Complex	Complex	Malignant
group				Cystic	EΗ	ΕH	EΗ	EΗ	
				glandular	Without	With	Without	With	
					atypia	atypia	atypia	atypia	
20-30	14	13				1			
31-40	31	10	6	2		9	3	1	
41-50	55	11	6	8	6	20	1	2	1
51-60	43	6	3	2	5	16	4	5	2
61-70	7	2			2		1	2	

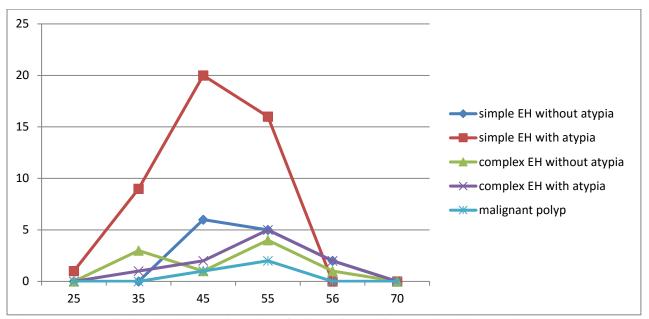


Figure 3: The age distribution with the histological findings of premalignant and malignant polyps.

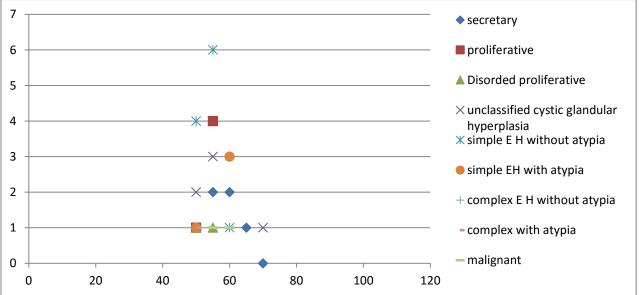


Figure 4: Histopathological types of polyp in post-menopausal women

polyp increases with increase age reaching the peak among women in their forth decade followed by fifth decade. Endometrial polyps are more common in premenopausal women, in whom they may present clinically as abnormal uterine bleeding menopause are linked to the development of endometrial polyps (24) which was near to our findings (74.6% were premenopausal and 25.4% were postmenopausal). Other study showed that it is much higher in postmenopausal in compare to premenopausal women (25). We found that hyperplastic polyps, the pre-malignant group, was highest in age group 51-60 years and the commonest subtype was endometrial hyperplasia with atypia seen in the 41-50 years age group. Three frank malignancy cases were found in these age groups suggesting that the perimenopausal period is the most critical period in term of risk of premalignant and malignant endometrial changes while a study conducted by Denise Hileeto et al showed that incidence od malignant endometrial polyp was highest in women aged more than 65 years although they had the lowest incidence of endometrial polyps. In our study, polyps were reported as benign in 49.3% of the cases while premalignant changes and malignant changes were found in 48.6% and 2% of the cases respectively while a study by Lee et al (15) reported a much lower prevalence of neoplasia (4.15%) in 194 women with symptomatic endometrial polyp presented with abnormal bleeding and other data showed the prevalence of endometrial neoplasia in these patients is low (1.15%) lower than our study (27) .Another study conducted by Wethington et al (28) noted that the risk of cancer or atypical hyperplasia was1% in premenopausal women with bleeding and 3.8% in postmenopausal women with bleeding.Other studies reported the malignant changes in endometrial polyps varying from 0 to 4.8% (29). The prevalence of premalignant and malignant polyp

changes varied in the included studies as 0.2-23.8% and 0-12.9%, respectively ⁽³⁰⁾.Ethnic variation could be implicated but there are no similar studies in Iraq or in neighboring countries to compare with.

REFERENCES

- 1. American Association of Gynecologic Laparoscopists: AAGL practice report: practice guidelines for the diagnosis and management of endometrial polyps. J Mini Invasive Gynecol. 2012 Jan-Feb; 19(1):3-10
- 2. U. Indraccolo, R. Di Iorio, M. Matteo, G. Corona, P. Greeco, S.R. Indraccolo: The pathogenesis of endometrial polyps: a systemic semi-quantitative review. Eur J Gynaecol Oncol. 2013;34(1): 5-22
- 3. Kitaya K, Tada Y, Taguchi S, Funabiki M, Hayashi T, Nakamura Y: Local mononuclear cell infiltrates in infertile patients with endometrial macropolyps versus micropolyps. Hum Reprod .2012 Dec;27(12):3474-80
- E. Dreisler, S. Stampe Sorensen, P. H. Ibsen, G. Lose: Prevalence of endometrial polyps and abnormal uterine bleeding in a Danish population aged 20-74 years. Ultrasound in Obstetrics & Gynecology. 2009 Jan;33(1):102-108
- Lieng M, Istre O, Sandvik L, Qvigstad E:Prevalence, 1-year regression rate, and clinical significance of asymptomatic endometrial polyps: cross-sectional study. J Minim Invasive Gynecol, 2009 Jul-Aug; 16(4):465-71
- M. Wong, B. Crenobrnja, V. Liberale, K. Dharmarajah, M. Widschwendter, D. Jurkovic:The natural history of endometrial polyps. Human Reproduction.2017 Feb;32(2):340-345
- Nigel Pereira, Allison C. Petrini, Jovana P. Lekovich, Rony T. Elias, Steven D. Spandorfer: Surgical Management of Endometrial Polyps in Infertile
- 8. Women: A Comprehensive Review. Surg Res Pract.2015;2015: 914390
- D. Keith Edmonds: Dewhurst's Textbook of Obstetrics & Gynaecology, 8th edition 2012:Chapter 54;Benign disease of the uterus: p.2016
- 10. Marco Antonio Lenci, Vanessa Alessandra Lui do Nascimento, Ana Beatriz Grandini, Walid Makin Fahmy, Daniella de Batista Depes, Fausto Farah Baracat, Reginaldo Guedes Coelho Premalignant and malignant lesions in endometrial polyps in patients undergoing hysteroscopic polypectomy.Einstein (Sao Paulo). 2014 Jan/Mar;12(1): 16-21
- 11. Barbara L. Hoffman, John O. Schorge, Karen D. bradshaw, Lisa M. Halvorson, Joseph I. Schaffer, Marlene M. Corton: Williams Gynecology study guide, 3rd edition, 2016;chapter 8: abnormal uterine bleeding: p.189
- 12. Shushan A , Revel A , Rojansky N. :How often are endometrial polyps malignant?. Gynecol Obstet Invest. 2004 Aug;58(4): 212-5
- 13. Gambadauro P, Martinez-Maestre MA, Schneider J, Torrejon R: Endometrial polyp or neoplasia? A casecontrol study in women with polyps at ultrasound. Climacteric. 2015 Jun; 18(3): 399-404

- 14. Alon Ben-Arie, Chen Goldchmit, Yosif Laviv, Roni Levy, Benjamin Caspi, Monica Huszar, Ram Dgani: The malignant potential of endometrial polyps. Eur J Obstet Gynecol Reprod Biol. 2004 Aug; 115(2): 206-210
- 15. Jian-Hua Wang, Jin Zhao, Jun Lin: Opportunities and Risk Factors for Premalignant and Malignant Transformation of Endometrial Polyp:Management Strategies. Journal of Minimally Invasive Gynecology. 2010 Jan; 17(1): 53-58
- 16.Lee SC, Kaunitz AM, Sanchez-Ramos L, Rhatigan RM:The oncogenic potential of endometrial polyps: a systemic review and meta-analysis. Obstet Gynecol. 2010 Nov:116(5): 1197-205
- 17. Giordano G, Gnetti L, Merisio C, Mepignano M: Postmenopausal status, hypertension and obesity as risk factors for malignant transformation in endometrial polyps. Maturitas. 2007 Feb;56(2): 190-7
- 18. Pergialiotis V, Prodromidou A, Siotos C, Frountzas M, Perrea D, Vlachos: Systemic hypertension and diabetes mellitus as predictors of malignancy among women with endometrial polyps: a meta-analysis of observational studies. Meopause. 2016 Jan;23(6):691-7
- 19. Leing M, Istre O, Qvigstad E:Treatment of endometrial polyps: a systematic review. Acta Obstet Gynecol scand. 2010 Aug;89(8): 992-1002
- 20. Santos L., Coutinho S., Assuncao N.: Case report of malignant endometrial polyps. Gynecol Surg. 2007 Jun;4(2): 127-129
- 21. Golan A., Cohen-Sahar B., Keidar R., Condrea A., Ginath S., Sagiv R.: Endometrial polyps: Symptomatology, Menopausal Status and Malignancy. Gynecol Obstet Invest. 2010;70: 107-112
- 22.S. Salim, H.Won, E.Nesbitt-Hawes, N. Campbell, I. Abobott: Diagnosis and Management of Endometrial Polyps: A Critical Review of the Literature. Journal of MinimallyInvasive Gynecology. 2011 Sep-Oct;18(5): 569-581
- 23. Alberto Daniele, Annamaria Ferrero, Furio Maggiorotto, Gaetano Perrini, Eugenio Volpi, Piero Sismondi: Suspecting Malignancy in Endometrial Polyps: Value of Hysteroscopy. Tumori Journal. 2013;99(2): 204-209
- 24. Kanthi JM, Remadevi C, Sumathy S, Sharma D, Sreedhar S, Jose A: Clinical Study of Endometrial Polyp and Role of Diagnostic Hyteroscopy and Blind Avulsion of Polyp. J Clin Diagn Res. 2016 Jan;10(6): QCO 1-4
- 25.J. Mark Cline, Laurie Brignolo, Elizabeth W. Ford. Nonhuman Primates in Biomedical Research (second edition) 2012, Chapter 10 Urogenital System; Pages 483–562.
- 26. Arie Lissak, MD. Incidence of Malignant and Premalignant Endometrial Polyp in Asymptomatic and Symptomatic Postmenopausal Women. Carmel Medical Center; 2014
- 27. Denise Hileeto, oluwole Fadare, Maritza Martel and Wenix Zheng. Age depend ent association of endometrial polyps with increased risk of cancer

- involvement. World Journal of Surgical Oncology.2005; 3(no.1):1-8
- 28.P. Gambadauro, M.A. Martinez-Maestre, J.Schneider & R. Torrejon. Malignant and premalignant changes in the endometrium of women with an ultrasound diagnosis of endometrial polyp. J Obstet Gynaecol. 2014 Oct;34(7): 611-615
- 29. Wethington SL, Herzog TJ, Burke WM, Sun X, Lemer JP, Lewin SN, Wright JD: Risk and predictors of malignancy in women with endometrial polyps. Ann Surg Oncol. 2011 Dec;18(13): 3819-23
- 30. Savelli L , De Iaco P, Santini D, Rosati F, Ghi T, Pignotti E, et al. Histopathologic features and risk factors for benignity, hyperplasia, and cancer in endometrial polyps. Am J Obstet Gynecol 2003;188(4):927-31.
- 31.Lieng M, Istre O, Qvigstad E. Treatment of endometrial polyps: a systematic review Medline ® Abstract for Reference 1 of 'Endometrial polyps' Department of Gynecology, Oslo University Hospital, Ullevål, Oslo, Norway. m.lieng@online.no. Acta Obstet Gynecol Scand. 2010 Aug;89(8):992-1002.