Clinico-pathologic Characteristics of Patients with Pre-operative Diagnosis of Endometrial Polyp who Underwent Hysteroscopy: A Review of Cases and a Search for Risk Factors for Malignancy

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Objectives: To determine the clinicopathologic characteristics of patients with pre-operative diagnosis of endometrial polyp who underwent hysteroscopy in the Philippine General Hospital and to identify possible risk factors for pre-malignancy and malignancy among patients with pre-operative diagnosis of endometrial polyp.
Study Design: Admission logbooks and surgico-pathologic census were analyzed to identify patients with a pre-operative diagnosis of endometrial polyp who underwent hysteroscopy from June 2009 to June 2014. Demographic, clinical and pathologic data were obtained and tabulated. Statistical analysis were performed to identify factors associated with pre-malignant and malignant lesion.
Results: A total of 180 patients were included in this study. Majority of the study population are below 50 years of age and are pre-menopausal. Eight cases were pre-malignant (n=2) and malignant (n = 6). Diabetes mellitus, tamoxifen use and prolapsed endometrial polyps were the variables associated with pre-malignant and malignant lesions. Diabetes mellitus was the only strong predictor for malignancy (OR = 6.83)
Conclusion: Endometrial polyps are benign endometrial overgrowths common among premenopausal women. Known risk factors for malignancy in cases of endometrial polyps include age, menopausal status, abnormal uterine bleeding, hypertension, diabetes mellitus, obesity and large size of endometrial polyp. In this study, only the presence of diabetes mellitus was interpreted as a significant predictor for either a pre-malignancy or malignancy.

Key words: endometrial polyp, hysteroscopy, malignancy

Introduction

Endometrial polyps are localized endometrial overgrowths which on histology should contain all of the following components: endometrial glands, endometrial stroma and blood vessels.[1] It has been suggested that estrogen stimulation of the endometrium plays an important role in the genesis of endometrial polyps.[2] However, its exact etiology remains to be unknown. Endometrial polyp usually presents with abnormal uterine bleeding, but with the increased use of pelvic sonography, incidental asymptomatic polyps are now becoming common.[3] The pattern of vaginal bleeding ranges from vaginal spotting to profuse vaginal bleeding. Aside from abnormal uterine bleeding, endometrial polyps can also present with prolapsing cervical mass and abnormal vaginal discharge.[2,4] It is rare among women less than

20 years old. Its incidence rises steadily with increasing age and peaks in the 5th decade of life.[4] According to the latest guideline of the American Association of Gynecologic Laparoscopists (AAGL), age is the most recognized risk factor for the development of endometrial polyp.[5] Other identified risk factors are Tamoxifen and hormone replacement therapy use, hypertension and increased body mass index (BMI).[6-11] Studies have also found an association between endometrial polyps and other gynecologic conditions such as myomas, cervical polyps and pelvic endometriosis.[5] Endometrial polyps have also been found during hysteroscopy in cases of infertility prior to their courses of In-Vitro-Fertilization (IVF).[12,13]

The management of endometrial polyps depends on the size and on the age of the patient. If the polyp is asymptomatic and less than 1 cm in size, conservative management is considered acceptable.[2,4,5] The presence of abnormal uterine bleeding, especially in the post-menopausal years is usually treated surgically, since the chances of malignancy is high.[5] Medical management of endometrial polyps still has limited role as of present.

Hysteroscopic polypectomy is the treatment of choice in managing endometrial polyps. During hysteroscopy, polyps can be removed electrosurgically or by removal through forceps and then re-visualization of the endometrial cavity by hysteroscopy. A monopolar or bipolar current can be used during electrosurgical removal of polyp.

One of the important reasons why endometrial polyps are being actively managed, aside from addressing the abnormal uterine bleeding, is to rule out malignancy. Several case series have reported as high as 12.9% incidence of malignancy arising from a pre-operative diagnosis of endometrial polyp.[5]

Hysteroscopy has been introduced in the Philippines in 1994. It is in the same year when the University of the Philippines-Philippine General Hospital had its first hysteroscopic procedure. Since then, there has been increasing trend in the use of hysteroscopy, specifically in the management of endometrial polyp.

This study will try to search for possible risk factors present among Filipinos with pre-operative diagnosis of endometrial polyp that will predispose them to malignancy.

Objectives

General Objectives

To determine the clinicopathologic characteristics of patients with pre-operative diagnosis of endometrial polyp who underwent hysteroscopy in the Philippine General Hospital.

Specific Objectives

1. To determine the clinical characteristics of patients with pre-operative diagnosis of endometrial polyp, who underwent hysteroscopy in the Philippine General Hospital in terms of the following variable:
   a) Age
   b) Menopausal status
   c) Parity score
   d) Presence of hypertension
   e) Presence of diabetes mellitus
   f) Tamoxifen use
   g) Chief complaint
   h) Pattern of menses
   i) History of infertility
   j) Body mass index
   k) Internal examination, specifically:
      i. Presence of prolapsing vaginal mass
      ii. Corpus size

2. To determine the sonographic findings patients with pre-operative diagnosis of endometrial polyp who underwent hysteroscopy in the Philippine General Hospital in terms of the following variable:
   a. Endometrial thickness
   b. Size of endometrial polyp
   c. Presence of other uterine pathology

3. To determine the intra-operative findings of patients with pre-operative diagnosis of endometrial polyp who underwent hysteroscopy in the Philippine General

Hospital in terms of the following variable:
   a. Size of mass
   b. Thickness of endometrium

4. To determine the histopathologic outcomes of patients with pre-operative diagnosis endometrial polyp who underwent hysteroscopy in the Philippine General Hospital.

5. To identify possible risk factors for pre-malignancy and malignancy among patients with pre-operative diagnosis of endometrial polyp.

Materials and Methods

Study Design and Population

This was a descriptive analytic study approved by the Expanded Hospital Research Office.

This study was a five-year review of all patients admitted from June 2009 to June 2014 who were pre-operatively diagnosed with endometrial polyp managed through hysteroscopy by the Section of Reproductive Endocrinology and Infertility at the Philippine General Hospital, This study did not include patients who have endometrial polyp only as their final histopathologic diagnosis and not as pre-operative diagnosis as well.

The admission logbook and surgico-pathologic census were the source of the patients that were included in the study. The investigators evaluated the completeness of the patient database forms, ultrasound and intra-operative findings, and histopathologic results of the study population. The following were the data extracted from the patients' records: age, menopausal status, obstetric score, presence of hypertension, presence of diabetes mellitus, Tamoxifen use, chief complaint, pattern of menses, history of infertility, body mass index, internal examination (presence of prolapsing vaginal mass and corpus size), sonographic findings (endometrial thickness, size of endometrial polyp and presence of other uterine pathology), intra-operative findings (size of mass and endometrial thickness) and histopathologic result. All data gathered were entered in a pre-made Excel worksheet. Data cleaning prior to data analysis was performed by checking the encoded data for missing values, inconsistencies, and miscoded data.

Statistical Analysis

All analyses were performed using Stata SE for Windows version 12.0. Descriptive statistics such as means and standard deviations for quantitative data, and frequencies and proportions for qualitative data were derived.

Simple logistic regression was used to determine the relationship between each of the independent variables and histopathologic findings. The significant predictors of a pre-malignant or malignant histopathologic findings were determined using multiple logistic regression. A beginning full model was fitted by combining the variables which were significant in simple logistic regression (a p-value of <0.25 was considered significant). The forward selection method was then used to determine which of the variables would be included in the final model.

Results

There was a total of 208 charity patients who underwent hysteroscopic polypectomy for endometrial polyp in the Philippine General Hospital over a 5-year period from June 2009 to June 2014 performed by the Fellows-in-Training of the Section of Reproductive Endocrinology and Infertility. Of which, only 180 patients (86.5%) have retrievable case records, ultrasound findings and histopathologic results. In all of the cases, the procedure was successful with the complete removal of the entire lesion.

Demographic and clinical characteristics of the study population are shown in Table 1. The mean age of the study population was 41.4. The youngest patient with endometrial polyp managed with hysteroscopy was 17 years old while the oldest was 74 years of age. Majority of patients (80.6%) were less than 50 years old and were pre-menopausal (82.8%). Only fifty two patients

(28.9%) were nulliparous and the rest were multiparous, with a mean gravidity score of 2.4 and parity score of 2. Only 23.3% (n = 42) have associated hypertension and only 5.6% (n = 10) have associated diabetes mellitus. Also, of the 180 patients, only 5 were on Tamoxifen as adjuvant treatment for their breast malignancy. Most of the patients consulted for abnormal uterine bleeding (89.4%), and the more common patterns of bleeding were described as either heavy (34.8%) or spotting (34.8%). Thirty one cases (17%) of endometrial polyp were associated with infertility, and most were cases of primary infertility.

Almost half (45.5%) of the study population have body mass indices above the normal values set by the World Health Organization for Asians (Table 2). Specifically, 19.4% were overweight, 18.3% were obese class I and 7.8% were obese class II. Based on their gynecologic examination, 42 cases of endometrial polyp (23.3%) presented with prolapsing mass below the cervix. There were 10 cases, which presented with large corpus size, and 11 (6.1%) cases with palpable adnexal masses.

Table 3 shows the sonographic findings of the study population. The mean size of endometrial polyp based on ultrasound was 27 mm. Majority of the endometrial polyps measured more than15 mm sonographically. The largest polyp measured was 134 mm, while the smallest measured was 6 mm. Multiple polyps were seen in twenty-five cases (13.9%). Almost 25% (n = 43) were associated with thickened endometrium on sonography. Other gynecologic conditions seen on ultrasound were myoma (n = 18), adenomyosis (n = 8), endometriotic cyst (7) and polycystic ovaries (n = 5).

Table 2. WHO BMI Classification for Asians.

Classification	BMI (kg/m^2)
Underweight	< 18.5
Normal	18.5 - 22.9
Overweight	23 - 24.9
Obese Class I	25 - 29.9
Obese Class II	>/= 30

Table 1. Clinical Characteristics of Study Population.

Variables	Values (Percentage)
Age	
≤50 years old	145 (80.6%)
>50 years old	35 (19.4%)
Menopause Status	
Pre-menopausal	149 (82.8%)
Post-menopausal	31 (17.2%)
Gravidity	Mean: 2.41 SD: 2.28 Range: 0 to 12
Parity	Mean: 2.01 SD: 2.07 Range: 0 to 10
Parity	
Nulliparous	52 (28.9%)
Multiparous	128 (71.1%)
BMI (*actual values*)	Mean: 23.02 SD: 3.92 Range: 13.2 to 35.6
BMI (classification)	
Normal	82 (45.5%)
Underweight	16 (8.9%)
Overweight	35 (19.4%)
Obese I	33 (18.3%)
Obese II	14 (7.8%)
Presence of Co-morbid conditions	
Hypertension	
Absent	138 (76.7%)
Present	42 (23.3%)
Diabetes Mellitus	
Absent	170 (94.4%)
Present	10 (5.6%)
Tamoxifen Use	
Absent	175 (97.2%)
Present	5 (2.8%)
Abnormal Uterine Bleeding	
Absent	19 (10.6%)
Present	161 (89.4%)
Type of with abnormal uterine bleeding (n=161)	
Heavy	56 (34.8%)
Prolonged	15 (9.3%)
Prolonged and Heavy	34 (21.1%)
Spotting	56 (34.8%)
History of Infertility	
Absent	149 (82.8%)
Present	31 (17.2%)
Type if with history of infertility (n=31)	
Primary	23 (74.2%)
Secondary	8 (25.8%)
Internal Examination	
Absent	138 (76.7%)
Present	42 (23.3%)
Corpus Size	
Small	170 (94.4%)
Large	10 (5.6%)
Adnexal Mass	
Absent	169 (93.9%)
Present	11 (6.1%)

Table 3. Sonographic findings of study population.

Variables	Values (Percentages)
Size of EM Polyp	
<10 mm	5 (2.8%)
11-15 mm	36 (20%)
>15 mm	139 (77.2%)
EM Thickness	
Thin	137 (76.1%)
Thick	43 (23.9%)
Number of Polyp	
Single	155 (86.1%)
Multiple	25 (13.9%)
Other Sonologic Findings	
Adenomyosis	8 (19.5%)
Dermoid cyst	1 (2.4%)
Endocervical polyp	1 (2.4%)
Endometriotic cyst	7 (17.1%)
Myoma	18 (43.9%)
Polycystic ovaries	5 (12.2%)
Paratubal cyst	1 (2.4%)

Table 4. Hysteroscopic findings of study population.

Variables	Values (Percentages)
Size of EM Polyp	
None	10 (5.6%)
<10 mm	10 (5.6%)
11-15 mm	31 (17.2%)
>15 mm	129 (71.7%)
EM Thickness	
Thin	94 (52.2%)
Thick	86 (47.8%)
Number of Polyp (n=170)	
Single	129 (75.9%)
Multiple	41 (24.1%)

Table 5. Histopathologic outcomes of study population.

Variables	Values (Percentages)
Benign vs Pre-malignant vs Malignant	
Benign	172 (95.6%)
Pre-malignant	2 (1.1%)
Malignant	6 (3.3%)
Benign vs Pre-malignant + Malignant	
Benign	172 (95.6%)
Pre-malignant + malignant	8 (4.4%)

Hysteroscopic findings of the subjects are presented in Table 4. The average size of endometrial polyp seen during hysteroscopy was 26 mm. Majority of the endometrial polyps measured more than 15 mm (71.2%). There were 10 cases wherein there were no endometrial mass appreciated on hysteroscopy, instead a fluffy endometrium was observed. In these cases, endometrial sampling was done with the final histopathologic reading still consistent with an endometrial polyp.

Table 5 shows the breakdown of the histopathologic findings of the study population. In general, 95.6% have benign findings. There were six cases of malignancies (3.3%) and two (1.1%) cases pre-malignancies. Of the 180 cases operated, 85.6% have histopathologic findings consistent with the pre-operative diagnosis of endometrial polyp. The other benign cases were mostly leiomyoma (n = 6), adenomyoma (n = 3), disordered proliferative phase endometrium (n = 3) and secretory phase endometrium (n = 3).

Of the six cases which turned out to be leiomyomas on biopsy, there is one case that made the surgeon changed the pre-operative diagnosis from endometrial polyp to leiomyoma since the mass was found to be more round and solid than fleshy. For the rest of the five cases, the surgeons maintained endometrial polyp as their final impression of the case. For the three cases with a final diagnosis of adenomyoma, all presented with an endometrial mass of equal or more than 2 cm. One of these cases had an associated adenomyosis on ultrasound. But none of these cases had the surgeon consider that it was not an endometrial polyp.

Of the six cases with a histopathologic reading of either secretory or disordered proliferative endometrium, only one presented with no definite endometrial mass and the rest had definite mass of at least one cm. Also, five of the six cases had an associated thickening of the endometrium. There

were two cases with a histopathologic finding of gestational endometrium, both of which had a previous history of abortion but with a negative pregnancy test. There was one case, which turned out to be fibroepithelial polyp. It presented with an 8 cm prolapsing mass from the cervix, which on hysteroscopy was noted to be attached at the isthmic region of the uterus.

Table 6 shows the clinicopathologic characteristics of patients whose histopathologic reading was signed out as pre-malignant or malignant lesion. Seven of the eight cases were pre-menopausal. Three (37.5%) had associated hypertension, and only two had diabetes mellitus. There is only one patient in this group on Tamoxifen. All eight cases complained of abnormal uterine bleeding, half of which presented with vaginal spotting. Aside from the distinct endometrial mass, there were no other ultrasound findings stated that would point to a malignancy. Of the malignant case, only two had the surgeons suspect of a possible malignancy since both presented with a large prolapsing endometrial mass, which was necrotic on cut section. In one of these cases, the surgeon sent the endometrial mass for frozen section which was initially read as endometrial polyp with hyperplastic changes. There is only one patient among the six cases of malignancy which presented with secondary infertility, thus completion surgery was not performed. This patient was placed on megestrol acetate 80 mg per day for 12 weeks. The rest of the patients underwent completion surgery in the form of exploratory laparotomy, extrafascial hysterectomy with bilateral oophorectomy bilateral lymph node dissection and para-aortic lymph node sampling. The final stagings of their endometrial malignancies are Stage IA (n = 2), Stage IB (n = 2) and Stage II (n = 1).

Table 7 shows the results of simple logistic regression analysis. It showed that the presence of diabetes mellitus is the only significant predictor of malignancy ($p < 0.031$). Also on multiple logistic regression analysis, as shown in Table 8, only the presence of diabetes mellitus which was found to be a significant predictor of both pre-malignant and malignant lesion, with an odds of having a malignant outcome when the patient has diabetes mellitus is 6.83.

Discussion

Endometrial polyp is a common gynecologic disorder, with a prevalence of 7.8 – 34.9%.[5] This incidence may actually be higher since most cases are asymptomatic and are routine findings during pelvic ultrasonography. [4] Risk factors that were identified for the development endometrial polyp include age, hypertension, obesity and tamoxifen use.[5]

According to the latest practice guideline of AAGL on endometrial polyp, increasing age during the reproductive years is the most common risk factor identified in patients with this gynecologic

Table 6. Clinicopathologic characteristics of patients with premalignant or malignant histopathologic readings.

Age	G/P	Meno-pausal Status	HPN	DM	Tamoxi fen	AUB	Type of AUB	Infer-tility	BMI	BMI Class	Prolap-sed Mass	Corpus Size	Adnex-al Mass	UTS size (cm)	UTS EMT	Other UTS Finding	Hystero EMT	Hystero EM	Histopathologic findings
66	G3P3 (3003)	Post	Absent	Absent	Absent	Present	Spotting	Absent	27.3	Obese I	Absent	Small	Absent	2.1	Thin	None	2	Thick, general	Endometrioid Adenocarcinoma FIGO 2
46	G0	Pre	Present	Present	Absent	Present	Prolonged and Heavy	Absent	27	Obese I	Present	Small	Absent	8.7	Thin	None	8	Thin	Endometrioid Adenocarcinoma, endometrioid type with squamous differentiation arising from EM polyp
39	G1P0	Pre	Present	Present	Absent	Present	Heavy	Absent	25	Obese I	Absent	Small	Absent	1.3	Thin	None	4	Thin	Endometrioid Adenocarcinoma FIGO 2
45	G0	Pre	Present	Absent	Absent	Present	Spotting	Absent	26	Obese I	Absent	Small	Absent	1.6	Thin	Myoma	3 – multiple x 3	Thick, general	Endometrioid Adenocarcinoma, well differentiated
23	G0	Pre	Absent	Absent	Absent	Present	Prolonged and Heavy	Absent	22.1	Normal	Present	Small	Absent	10.5	Thin	None	10	Thick, focal	Adenosarcoma
35	G1P0 (0100)	Pre	Absent	Absent	Absent	Present	Spotting	Presen t	21	Normal	Absent	Small	Absent	5.4	Thin	Myoma	3 – multiple x 4	Thick, focal	Adenosquamous carcinoma FIGO 2
41	G1P0	Pre	Absent	Absent	Absent	Present	Heavy	Presen t	26.7	Obese I	Present	Small	Absent	3.9	Thick	None	4	Thin	Complex atypical hyperplasia
47	G3P3 (3003)	Pre	Absent	Absent	Present	Present	Spotting	Absent	19.6	Normal	Present	Small	Absent	5	Thin	None	5	Thin	EM polyp with Complex atypical hyperplasia

Table 7. Simple logistic regression analysis.

Variables	Odds Ratio (95% CI)	p-value
Age	0.58 (0.07 - 4.87)	0.616
Menopause status	0.68 (0.08 - 5.70)	0.719
Parity	0.66 (0.15 - 2.89)	0.585
Body mass index	1.31 (0.80 - 2.15)	0.277
Hypertension	2.05 (0.47 - 8.95)	0.341
Diabetes mellitus	6.83 (1.19 - 39.35)	0.031
Tamoxifen use	6.00 (0.59 - 60.94)	0.130
Abnormal uterine bleeding	Sparse data	-
History of infertility	1.64 (0.32 - 8.550)	0.555
Prolapsing mass	3.53 (0.84 - 14.76)	0.085
Corpus size	Sparse data	-
Adnexal mass	Sparse data	-
Size of EM polyp (sonographic)	2.13 (0.29 - 15.61)	0.458
EM thickness (sonographic)	0.44 (0.05 - 3.70)	0.451
Number of polyp (sonographic)	Sparse data	-
Size of EM polyp (hysteroscopic)	Sparse data	-
EM thickness (hysteroscopic)	1.87 (0.43 - 8.08)	0.401
Number of polyp (hysteroscopic)	1.96 (0.45 - 8.57)	0.373

*All significant variables (p-value <0.25) will be included in the full model of MLR.

Table 8. Multiple Regression Analysis.

Variables	Odds Ratio (95% CI)	p-value
Diabetes mellitus	6.83 (1.19 - 39.35)	0.031

pathology. Among the 180 subjects in this study, the mean age was 41.4 years old and majority (81%) are less than 50 years of age. This is contrary to the statement of the Royal College of Obstetrician and Gynecologists which states that the incidence of endometrial polyp peaks at the fifth decade of life. It is very rare among women less than 20 years of age, but this study was able to find one case of endometrial polyp in a 17 year old presenting with heavy menstrual bleeding.

Advanced age is also considered a risk factor for the development of atypical hyperplasia and malignancies arising from endometrial polyps. This has been observed in several studies such that of Hileeto et al [14] on 513 cases with pre-operative diagnosis of endometrial polyp who underwent endometrial curettage or hysterectomy, of which sixty-six cases turned out to be malignant. The study observed a higher rate of malignancy (55%) among patients more than 65 years old compared to those with age 56 – 65 years old (17%) and 46 – 55 years old (15%). Baiochi, et al.[15] had also the same finding when their group did a 12-year review on 1,242 patients who underwent hysteroscopy for endometrial polyp. They noted that patients who are more than 60 years of age were more frequent to have a pre-malignant or malignant lesion. This was also the same observation by the group of Savelli.[16] The group reviewed 509 patients with endometrial polyp who underwent hysteroscopy. Twenty patients had either a pre-malignant or malignant histopathologic reading. They noted that patient's age (mean = 64.4 years old) as one of the characteristics associated with either a pre-malignant or malignant histopathologic finding. Also, in a same study performed by Costa-Paiva et al on 870 women, age was noted to be significant

risk factor for malignancy.[17] They noted that prevalence rates of malignant polyps were 3.7% in women younger than 40 years, 3.11% in women aged between 40 and 59 years, and 5.36% in women older than 60 years. The findings of these studies were not the same with the present one. Of the eight cases which were either pre-malignant or malignant, only one patient was older that 50 years old. The absence of statistical significance for age as a factor can be attributed to the small number of both the study population and the malignant cases compared to the other studies.

Endometrial polyps are more common in the pre-menopausal women than in the post-menopausal group.[14,18] This was observed in this present study, with 83% of the study population being pre-menopausal. Endometrial malignancies on the other hand are more common among the post-menopausal women.[19] In this study, there was no significant association between menopausal status and a pre-malignant or malignant histopathologic finding. This was also the same finding of a meta-analysis performed by Lee, et al. on the oncogenic potential of endometrial polyp.[2] The study included a total of 10,752 patients who underwent polypectomy for endometrial polyp. Of these, 377 cases had malignant biopsies and menopausal status was not proven to be a significant factor to predict malignancy. Unlike in a smaller study by Wethington, et al. on 509 women who underwent hysteroscopy for endometrial polyp, in which 20 cases turned out to be malignant, they noted a significant association between patients who are post-menopausal and malignancy.[20] This was also the finding of the study by Baiochi, et al. which was earlier mentioned. They noted that those who are post-menopausal, are more common to have a pre-malignant or malignant biopsy (82%), and this was statistically significant.[15]

Endometrial polyps are generally asymptomatic, but in symptomatic cases, they present with heavy menstrual bleeding in 50% of pre-menopausal patients.[4] In this study, 89% presented with abnormal uterine bleeding. The most common pattern of bleeding was described as heavy (35%) and spotting (35%). All of the eight cases which were pre-malignant and malignant presented with abnormal uterine bleeding, however on statistical analysis, the relationship between the said symptom and malignancy was not statistically significant. This is in contrary to findings of the study of the groups of Lee, Baiochi and Costa-Paiva, which showed that the presence of abnormal uterine bleeding is associated with malignancy.[2,15,17] Specifically, the meta-analysis of Lee, et al. demonstrated that abnormal uterine bleeding among post-menopausal women is a significant predictor for malignancy.[2]

The presence of hypertension is also considered as a risk factor for any hormone-dependent new growth in women, whether benign or malignant because it promotes a decrease in the mechanisms of cell apoptosis, therefore favoring tumor growth.[21] In this study, only 23.3% (n=42) of the subjects were hypertensive, and it was not identified as a significant predictor for malignancy. This is contrary to the studies of the Baiochi, et al.[15], Paiva, et al. and Savelli, et al. which were previously mentioned. The group of Baiochi noted that 71.1% (32 of 45 cases) of their subjects who had a pre-malignant or malignant lesion were hypertensive, and it was statistically significant. The group of Costa-Paiva [17] also noted a significant association of the presence of hypertension in predicting malignancy when simple linear regression analysis was used. Savelli,[16] et al. also found hypertension, together with age and menopausal status, as previously described, are significant risk factors for patients to have a pre-malignant or malignant histopathologic outcomes.

Patients with associated diabetes mellitus are at increased risk to develop to endometrial carcinoma mainly because of hyperinsulinemia.[22] In patients with diabetes mellitus, both insulin and the IGF-1 are elevated. These two function in an integrated fashion to promote cell growth and survival, and with chronic exposure can enhance carcinogenesis. This present study found that diabetes mellitus is a significant predictor for malignancy. Specifically this study was able to demonstrate that the odds of developing a pre-malignant or malignant outcome are 6.83 times higher among those patients with diabetes mellitus. The other similar studies that have been mentioned found no significant association

with the presence of diabetes mellitus and a malignant lesion.

The use of tamoxifen is a known risk factor both for the development of endometrial polyp and endometrial carcinoma. Tamoxifen are selective estrogen receptor modulator, and have mixed estrogenic and anti-estrogenic activity thus can stimulate endometrial proliferation.[1] In the present study, only 5 of the 180 patients (2.8%) were on tamoxifen. Of this five users, one (20%) had a histopathologic reading of endometrial polyp with atypical hyperplasia. This study was not able to find significant association with Tamoxifen use and malignancy. This was also the result of the study by Ben-arie, et al.[24] on 420 patients of endometrial polyp who underwent hysteroscopy. Among these patients, only 18 were Tamoxifen users, and there was no significant association seen between the two variables. The study of Baiochi, et al.[15] which have been repeatedly mentioned in this paper also found the same findings.

Obesity is also a known risk factor for both endometrial polyp and endometrial carcinoma. Obesity has been associated with elevated endogenous estrogen levels, decreased levels of sex hormone-binding globulin, and reduced progesterone production, all of which favors the development of endometrial malignancy.[23] Using the WHO BMI classification for Asians (Table 2), 46% of the study population have a BMI above the normal. Among those who had a pre-malignant or malignant lesion, 5 out of 8 (62.5%) were obese class I. However, there was no significant association seen with obesity and development of malignancy in this study. The absence of significant association between obesity and malignancy in this study can be explained by the big percentage of the whole study population being overweight and obese already and not just those who were diagnosed malignancy. This was also the case with the other studies that have been mentioned except for the study by Paiva et al. They noted that obesity can be a predictor of malignancy when simple logistic regression analysis was done but not when multiple logistic regression was utilized.

The size of endometrial polyp is one of the factors that are being considered if conservative, meaning expectant management can be done. It is more likely that the polyp will regress if it is less than 10mm. The size of endometrial polyp is also considered a predictor for malignancy.[4,24,25] For the present study, majority (77%) of cases were more than 15mm in size. Of the pre-malignant and malignant cases, all polyps measured more than 15mm. However, this study found no significant association between the size of the endometrial polyp and malignancy. This is in contrary to the study of Paiva, et al. wherein endometrial polyps more than 15 mm were associated with an increased risk for malignancy.[17] Ferrazi et al also have the same finding, but the size of the endometrial polyp that they found to have strong association with malignancy was more than 18 mm.[25] Also, since most of the endometrial polyps in this study were more than 15 mm, it is expected that there will be large number that will present as a prolapsing mass outside of the cervix. In this research, 23% (n=42) presented with a prolapsed endometrial mass. Among the pre-malignant and malignant cases, three of the eight cases presented with prolapsed mass. However there was no statistically significant association between the presence of a prolapsed endometrial mass and malignancy. No other studies have considered the presence of prolapsed mass as possible risk factor for the malignant transformation of endometrial polyp.

Conclusion and Recommendation

Endometrial polyps are benign endometrial overgrowths common among the premenopausal women. Risk factors for its development include increasing age, hypertension, obesity and tamoxifen use, and these were all appreciated in this study. Risk factors for malignancy in cases of endometrial polyps include age, menopausal status, abnormal uterine bleeding, hypertension, diabetes mellitus, obesity and large size of endometrial polyp. In this study, only the presence of diabetes mellitus was interpreted as a significant predictor of malignancy in patients with pre-operative diagnosis of endometrial polyp. Therefore, the

presence of diabetes mellitus, regardless of the other factors should be considered in removing an endometrial polyp.

The authors recommend a similar but larger multicenter study.

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