ORIGINAL ARTICLE

Spectrum of Pathological Lesions in Uterine Specimens with Focus on Gestational Trophoblastic Disease in Karachi

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ABSTRACT

Background: The most common benign pathological lesion in women of reproductive age is uterine leiomyoma. Gestational trophoblastic disease includes tumors and tumor like lesions originating from trophoblastic tissue. The aim of this study was to find the spectrum of molar pregnancy and uterine pathologies focusing on gestational trophoblastic disease as no study has been done in the past few years.

Methods: Endometrial and uterine specimens of patients (n=436) between the ages of 15-65 years were collected from a private hospital in Karachi from December 2018 to December 2019. This cross-sectional study was carried out by pathological diagnosis of patients' samples under light microscopy using hematoxylin and eosin staining. Stratification was done about age and nature of specimen to control the effect modifiers. The post stratification Chi square test was applied and *p* value <0.05 was considered significant.

Results: Mean age of the patients was 36.1 years ±7.8. Total 436 uterine biopsies included 260(59.6%) hysterectomies, 56(12.8%) endometrial curetting's, 117(26.8%) evacuation specimens and 3(0.7%) polypectomies. Common pathologies included 124(28.4%) leiomyomas, 61(14%) proliferative endometrium, 52(11.9%) adenomyosis and 32(7.3%) endometrial polyps. Gestational trophoblastic disease was seen in 9(2.06%). Seven (87.5%) were partial hydatidiform moles, one (12.5%) exaggerated placental site reaction and one choriocarcinoma. Mole was common between 26-30 years with mean age of 27.2 years and prevalence was 6/100 abortions.

Conclusion: Leiomyoma was the commonest (28.4%) uterine pathology followed by proliferative endometrium (14.5%). However, endometrial stromal sarcoma and endometriosis were found 0.2% each. High prevalence of mole was seen in this study. Partial mole was most common and choriocarcinoma was least common.

Keywords: Hydatidiform Mole; Pathology; Prevalence.

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INTRODUCTION

Gestational trophoblastic disease (GTD) includes tumors that originate from the epithelium of trophoblast in the placenta surrounding the blastocyst. It is the result of abnormal growth of trophoblastic cells. GTD may occur after any antecedent pregnancy or it may follow a mole[1,2]. According to WHO classification, GTD comprises neoplastic lesions, non-neoplastic lesions, molar pregnancies, and non-molar villous lesions. Neoplastic lesions include choriocarcinoma, placental site trophoblastic tumor and epithelioid trophoblastic tumor. Non-neoplastic lesions include exaggerated placental site reaction

(ESPR), placental site nodule and plaque[3]. Hydatidiform mole (HM) is the most common entity of GTD and it can be complete, partial or invasive.

The incidence of molar pregnancy in different regions of the world varies. The incidence of molar pregnancy is about 1/1000 pregnancies in European countries, 2 /1000 pregnancies in the region of Southeast Asia and Japan. In Taiwan, it is 1 /125 pregnancies[4-6]. The incidence of gestational trophoblastic neoplasia in Malaysia is 1.59/1000 deliveries[6]. A study in Turkey reported an incidence of 12.1 /1000 deliveries, which is the highest among all[7]. This difference is due to variations in data reporting, whether the study is population-based or hospital-based.

The higher incidence in women may be attributable to their nutritional and socioeconomic status[8]. Risk factors for molar pregnancy are extreme maternal age (<15 years and >45 years), previous history of HM, low dietary carotene, and animal fat consumption[9,10]. Women aged more than 45 years have more than hundred-fold risk of complete mole than women do of 20-40 years age. Women with a previous molar pregnancy are also at risk. The risk of an HM increases to 1-2% in the next pregnancy following a molar pregnancy[11].

The complete HM is diploid and shows diffuse hydropic chorionic villi with trophoblastic hyperplasia and no fetus. Beta human chorionic gonadotrophin (β-hCG) is markedly elevated and women most commonly present with vaginal bleeding. Partial mole is usually triploid; fetus is present and the placenta is large. The hydropic villi are interspersed with normal chorionic villi[12,13]. Majority of the molar pregnancies when diagnosed are asymptomatic. Maternal age and β-hCG play an important role in the diagnosis[14]. On ultrasound, gestational sac is not seen in a complete mole. In partial mole, the ultrasound findings are very similar to a normal conception, so it is not easy to diagnose it initially. Later, these women present with loss in early pregnancy[15,16].

Choriocarcinoma is a malignant trophoblastic tumor that develops from villous cytotrophoblastic cells[16]. Majority of choriocarcinomas occur after a molar pregnancy[17]. The reported incidence of choriocarcinoma in United States is about 1 / 20,000 to 40,000 pregnancies and in Southeast Asia; it is 3 to 9 / 40,000 pregnancies[18]. Placental site trophoblastic tumor (PSTT) is composed of mononuclear intermediate trophoblasts infiltrating the myometrium in sheets or cords. Immunohistochemical staining of the tumor shows diffuse staining for cytokeratin and human placental lactogen. Cytogenic studies have shown diploid nature of these tumors[3]. Epithelioid trophoblastic tumor (ETT) develops from intermediate trophoblasts of chorionic type. Most ETTs follow a full-term delivery[3]. Other pathologies encountered in gynaecological specimens include leiomyomas, adenomyosis, endometrial polyp, proliferative and secretory endometrium, endometrial hyperplasia and endometrial carcinoma[19]. Therefore, the study aim was to analyze the spectrum of molar pregnancy and other uterine pathologies since, there has been no significant studies conducted in Pakistan within the past few years.

METHODS

This was a cross sectional study carried out at a private hospital in Karachi from December 2018-December 2019 after approval by institutional ethical review committee (Ref no. 1/2018). All the endometrial and uterine specimens of patients between the ages of 15-65 years, received at the hospital were collected. Data collected during the study period included: patient's age, specimen type, clinical history/diagnosis, and histological diagnosis. The tissue sections cut from the paraffin blocks were 3-4µm in thickness. Pathological diagnosis was done on light microscopy using routine hematoxylin and eosin staining technique. Two consultant histopathologists examined the histological slides independently.

The criteria that were used for the diagnosis of hydatidiform mole included the distribution and amount of trophoblastic proliferation, size of villi, villous edema with presence or absence of cistern formation and whether fetal tissue was present or absent[3]. Data was entered in SPSS version 20 and data analysis was done. Categorical variables like specimen type, clinical diagnosis and histological diagnosis were summarized into percentages, and mean (standard deviation) was calculated for numerical variable like age distribution. Stratification was done concerning age and nature of specimen to control the effecting modifiers. Post stratification, Chi square test was applied and p value < 0.05 was considered significant.

RESULTS

A total of 436 specimens were received during the study period which included 260 hysterectomy specimens (59.6%), 56 diagnostics endometrial curettings (12.8%), 117 uterine evacuation specimens (26.8%) and 3 polypectomies (0.7%). Out of the 117 (26.8%) cases of uterine evacuation, 7.6% presented as incomplete abortion and 58.1% presented with the complaint of vaginal bleeding and 6.8% cases of gestational trophoblastic disease were encountered. The relation between nature of specimen and GTD was statistically significant and p value was less than 0.05 in this study. The Hydatidiform Mole (HM) was seen in seven (87.5%) cases (Figure 1a, b) and one (12.5%) case of EPSR (Figure 1c) was seen. A single case of choriocarcinoma was diagnosed (Figure 1d) in hysterectomy speci-

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men (Table 1) of a 25 years old age group. Majority of uterine specimens (22%) received were of the patients in the age group of 36-40 years. Mean age with standard deviation of all the patients was 36.1 years ±7.8. HM was seen predominantly in women between 26-30 years and mean age of these women was 27.2 years. All moles were partial hydatidiform moles. The relation between age group of women and trophoblastic disease was not statistically significant in this study.

Table 1: Frequency of gestational trophoblastic disease (GTD) in different age groups and type of specimen found GTD positive.

Age Groups (years)	Other Pathologies (n)	Type of Gestational Trophoblastic Disease			*p*-Value
		Choriocarcinoma (n)	EPSR (n)	HM (n)	
Less than 20	4	0	0	0	0.15
21 - 35	128	1	1	7	
36 - 50	213	0	0	0	
51 - 65	2	0	0	0	
GTD Positive Specimen					
Endometrial curettings	56	0	0	0	0.007
Uterine evacuation	109	0	1	7	
Hysterectomy	259	1	0	0	
Polypectomy	3	0	0	0	

Exaggerated placental site reaction (ESPR), Hydatidiform mole (HM)

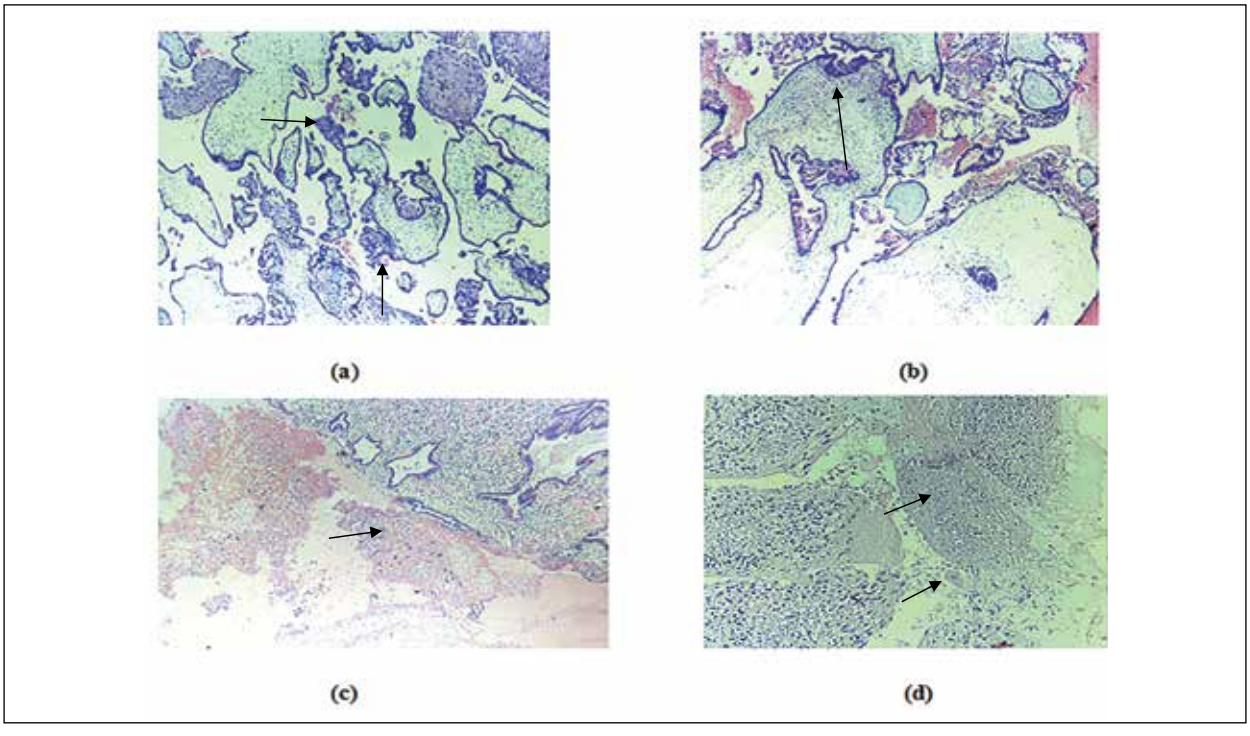

Figure 1: (a, b) Arrow shows Partial mole, showing focal proliferation of trophoblasts (c) Exaggerated placental site reaction, invasion of trophoblastic cells in endometrium (d) Choriocarcinoma showing intricate mixture of cytotrophoblasts and syncytiotrophoblast with areas of necrosis.

The prevalence of molar pregnancy was calculated by dividing the number of moles by cases of histologically diagnosed products of conception. It was 6 per 100 abortions. Commonly seen uterine pathologies on histopathological examination (Table 2) included 124 (28.4%) leiomyomas, 61(14%) cases of proliferative phase endometrium, 52(11.9%) adenomyosis and 32 (7.3%) endometrial polyps.

Table 2: Frequency of other uterine pathologies.

Uterine Pathologies	n	Percentage (%)	Uterine Pathologies	n	Percentage (%)
Leiomy oma	124	28.4	Adenomyoma	2	0.4
Adenomyosis	52	11.9	Chronic endometritis	2	0.4
Endometrial polyp	32	7.3	Decidual tissue	2	0.4
Proliferative endometrium	63	14.5	Endometrial carcinoma	2	0.4
Products of conception	104	23.9	Endometrial hyperplasia	3	0.7
Secretory endometrium	19	4.3	Procidentia uterus	2	0.4
Low grade Endometrial Stromal Sarcoma	1	0.2	Disordered proliferative endometrium	4	0.9
Inactive glands	14	3.1	Endometriosis	1	0.2

DISCUSSION

In this study, we observed nine cases of GTD out of 436 gynaecological specimens that were received. All nine cases were intrauterine since, there was no case of extrauterine GTD. The global prevalence of molar pregnancy is almost 1 for 4 abortions (24.7%) [20]. The prevalence of GTD in present study was 6 per 100 abortions. A study done by Mulisya in 2018 showed that the prevalence of hydatidiform mole was 6.1% [21]. This is very similar to the findings in our study and may be due to the poor nutritional and socioeconomic status of women in these areas.

The present study showed that women diagnosed with GTD ranged from 21 to 35 years. It is common in reproductive years attributable to the nutritional status of women in this group. GTD was most observed commonly in women between the age group of 21-30 years with eight cases (88.9%) and a single case (11.1%) was seen in the age group of 31-35 years. There was no case of GTD below 20 years in our study. Taboo showed that highest incidence of GTD was in the 20-25 years age group[22]. Thus, 66% women aged 20-25 years had GTD as reported in another study by Kumar et al., carried out in India[23]. The mean age of women with GTD in our study was 27.2 years, which showed concordance with other studies by Mayun and Moodley et al., noted the mean age of women as 25.7 and 28.5 years[24,6]. The *p* value was >0.05 and the relation between age groups and trophoblastic disease were not significant in this study. Extremes of age are a risk factor for molar pregnancy. However, the occurrence of GTD at an early age may be due to early marriage of females in our country.

The complete hydatidiform mole is diploid. Microscopic examination shows diffuse hydropic chorionic villi with trophoblastic hyperplasia and no fetus. The partial hydatidiform mole is usually triploid. The hydropic villi are seen interspersed with normal chorionic villi and fetal tissue is identified. Majority (87.5%) cases of GTD in our study were hydatidiform moles. Similar results were noted in other studies[25,26], partial moles being the most common entity among all the other gestational trophoblastic diseases, comprising 77.8%. A study in West Indies showed that partial moles made up 61.1% of the molar pregnancies[27]. Concordance with this study may be due to the similarity in classification and diagnosis of mole. Another study[23] showed that complete moles were more common than partial moles. Molar pregnancy was suspected clinically in eight patients out of 117 in our study and 7 were confirmed as hydatidiform moles histologically.

Hydatidiform moles show genetic abnormalities and there is risk of malignant transformation. Reassurance and close monitoring are needed in simple cases if there is no indication for additional treatment. Immunostaining with p57KIP2 is a new diagnostic test and helps to confirm the diagnosis of complete mole. P57 is the gene product of maternally expressed cyclin dependent kinase inhibitor gene CDKN1C. It is located on chromosome 11p15.5 and is not expressed in the stroma of complete hydatidiform mole[28,29].

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Since, choriocarcinoma is an aggressive malignant trophoblastic tumor. It can occur with or without pregnancy. About 50% of all choriocarcinoma follow a complete molar gestation and 25% follow a normal pregnancy. The remaining 25% arise after a miscarriage or an ectopic pregnancy. Histopathologic examination shows malignant proliferation of biphasic trophoblastic population. Hemorrhage and necrosis are extensive while gestational choriocarcinoma is chemoresponsive[16,17]. In this study out of nine cases of gestational trophoblastic disease, there was a single case of choriocarcinoma, constituting 11.1%. The patient was 25 years old and presented with vaginal bleeding.

The most common benign neoplasm in women of reproductive age group is uterine leiomyoma. The mode of therapy in uterine leiomyoma is hysterectomy. In the current study the commonly seen uterine pathologies on histopathological examination included 124 (28.4%) leiomyomas, 61(14%) cases of proliferative phase endometrium, 52(11.9%) adenomyosis, 32 (7.3%) endometrial polyps, 18 (4.1%) cases showing early secretory endometrial pattern, 14 (3.1%) showing inactive endometrium and disordered proliferative endometrial pattern was seen in 0.9%. Leiomyomas were seen predominantly (27.4%) in the age group of 36-40 years. The most common endometrial pattern observed in this study was proliferative endometrium.

Therefore, we may suggest that all products of conception should be sent for histological examination routinely due to high prevalence of molar pregnancy, especially if there is high clinical suspicion and risk factors like advanced maternal age, advanced gestational age and history of previous abortion is present. In addition, hysterectomy specimens may be carefully examined to confirm the diagnosis and to rule out malignant lesions.

CONCLUSION

Leiomyoma was the most common uterine pathology encountered at histopathology followed by proliferative phase endometrium. Furthermore, hydatidiform mole showed high prevalence among all gestational trophoblastic diseases. In addition, partial hydatidiform mole was the most common entity in this study. Thus, histopathological examination may be required for further diagnosis.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS APPROVAL

The study conducted at a private hospital in Karachi from December 2018-December 2019 with an approval by institutional ethical review committee (Ref no. 1/2018).

PATIENT CONSENT

They authors obtained the written consent from the patients.

AUTHORS' CONTRIBUTIONS

All authors equally contributed in this research manuscript.

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