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Gestational Trophoplastic Disease in Babylon Maternity and Paediatrics Teaching Hospital a Prospective Study

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Abstract:

Background: *Gestational trophoblastic tumours arise from the cells of conception and form a range of related conditions, from the benign partial mole to the aggressive malignancies of choriocarcinoma and placental site tumours. Despite the rarity of them, patients with molar pregnancies requiring additional treatment after evacuation can expect cure rate 100%.*

Objectives: *In the present study, we evaluated six years period of trophoblastic diseases in women attending Babylon Maternity and Paediatrics Teaching Hospital in prospective study.*

Patients & Method: *This study was a descriptive observational study, conducted from January 2008 until January 2014 in Babylon Maternity and Paediatrics Teaching Hospital, all cases with molar pregnancy been involved, after diagnosis been treated and followed up. Those with persistent high hCG referred for chemotherapy.*

Results: *Our study involved 83 patients with trophoblastic disease.The overall mean age was (28.40±8.89) years old and (24.1%) of patients were older than 35 years. In our study 83 patients with trophoblastic disease 74 of them were having complete hydatidiform mole (89.2%), four patients (4.8%) having partial mole, four patients with invasive mole (4.8%) and one patient with choriocarcinoma (1.2%).Regarding parity ranged from (0 – 8)para, 28 patients (33.8%) their parity were less than three, meanwhile 55 patients (66.3%) their parity more than three.About patient's residence in our study 56 patients (67.5%) were from rural area, meanwhile, 27 patients (32.5%) were from urban area.In this study, 83 women with trophoblastic disease six of them ended by hysterectomy(7.2%), 74 women with complete hydatidiform mole suction curettage performed for them only one patient ended with hysterectomy. Regarding chemotherapy 16 patients (19.3%) out of 83 received chemotherapy eleven after complete hydatidiform mole for persistent high hCG forming (8.14%), four patients with invasive mole and one case choriocarcinoma, while 67 patients (80.7%)*

did not received any chemotherapy.Regarding serum B-hCG levels pre-evacuation in our study for complete hydatidiform mole mean (29540+-26151) mIU/ml, for partial mole more than 20000mIU/ml, for invasive mole more than 30000 mIU/ml and for choriocarcinoma more than 100000 mIU/ml.
Conclusion: *Trophoblastic diseases occur during the fertility age mostly, and there is an increased risk with extreme of age and more previous pregnancies;Hydatidiform mole was thecommonest type of trophoblastic disease in these patients.(19.3%) of the patients necessity to chemotherapy.*
Key words: *Gestational trophoblastic disease, hydatidiform mole.*

INTRODUCTION

Gestational trophoblastic disease (GTD) arise from cells of conception (1) and forms a group of disorders spanning the conditions of complete and partial molar pregnancies through to the malignant conditions of invasive mole, choriocarcinoma and the very rare placental site trophoblastic tumour (PSTT). There are reports of neoplastic transformation of atypical placental site nodules to placental site trophoblastic tumour. If there is any evidence of persistence of GTD, most commonly defined as a persistent elevation of beta human chorionic gonadotrophin (hCG), the condition is referred to as gestational trophoblastic neoplasia (GTN)(2).Incidence of molar pregnancies in Europe and North America in the order of 0.2 – 1.5 per 1000 live births. There is variation in the incidence based on race and geography (1). The incidence of the malignant forms of GTD is much lower, only about 10% of the incidence of hydatidiform mole(3).There are two clearly documented risk factors for an increased risk of molar pregnancy: the extreme of maternal age and a previous molar pregnancy (1) .Although molar pregnancies affect women of all ages, women under 16 years of age have a six times higher risk of developing a molar pregnancy than those aged 16–40 years, and women 50 years of age or older have a one in three chance of having a molar pregnancy. Being from Asia/of Asian ethnicity is an important risk factor. (4)

In Complete hydatidiform moles the genetic material is totally paternal in origin, have no foetal tissue and no maternal DNA. A single sperm duplicates and this duplicated sperm fertilises an empty ovum, or, two sperms fertilise an empty ovum (dispermic fertilisation).The chromosome complement is most commonly 46XX.Partial hydatidiform moles have a foetus or foetal cells. They are triploid in origin with 69 chromosomes, one set of maternal haploid genes and two sets of paternal haploid genes. They almost always occur following dispermic fertilisation of a normal ovum. (1)

The patient presented with vaginal bleeding, enlarged uterus, pelvic pain or discomfort, and hyper emesis are the most common symptoms of GTD. Rarer presentations include hyperthyroidism, early onset pre-eclampsia or abdominal distension due to theca lutein cysts. Very rarely, women can present with acute respiratory failure or neurological symptoms such as seizures; these are likely to be due to metastatic disease. (2)

The role of hCG in trophoblast disease diagnosis: It is produced by synctiotrphoblast cells, hCG is a glycoselated hetero dimmer protein consisting of alpha and beta subunits held together by non –covalent

bonds. In malignant disease a number of hCG variants can occur including hyperglycoselatedhCG, nicked hCG, hCG missing the beta subunit C terminal peptide and the free beta subunit. In GTD it is elevated and the diagnosis confirmed by histo-pathological exam. which can be done after evacuation of molar pregnancy, in cases of choriocarcinoma elevated serum hCG usually make the diagnosis clear and so avoid biopsy ,which can be hazardous due to risk of severe haemorrhage. (1)

Treatment is always necessary. It consists for hydatidiform mole theevacuation of pregnancy. (5), this will lead to the relief of symptoms, and prevent later complications. Suction curettage is the preferred method of evacuation. Hysterectomy is an alternative in some cases. Hydatidiform mole also has successfully been treated with systemic methotrexate (6).While the treatment for invasive mole or choriocarcinoma is the same, both are usually treated with chemotherapy. Methotrexate and Dactinomycinare among chemotherapy drugs used in GTD (7), only a few women suffer from poor prognosis those with metastatic gestational trophoblastic disease. Radiotherapy can also be given to places where the cancer has spread, as the brain (8). Women who undergo chemotherapy are advised not to conceive for one year after completion of treatment. These women also are likely to have an earlier menopause. It has been estimated by the Royal College of Obstetricians and Gynaecologists that the age at menopause for women who receive single agent chemotherapy is advanced by one year and by three years for women who receive multi agent chemotherapy(2). Follow up is necessary in all women with gestational trophoblastic disease, because of the possibility of persistent disease, or because of the risk of developing malignant uterine invasion or malignant metastatic disease even after treatment in some women with certain risk factors (9) .Follow up after GTD is increasingly individualised. If hCG has reverted to normal within 56 days of the pregnancy event then follow up will be for 6 months from the date of uterine evacuation. If hCG has not reverted to normal within 56 days of the pregnancy event then follow-up will be for 6 months from normalisation of the hCG level. The use of a reliable contraception method is very important during the entire follow up period, because the follow-up depends on measuring hCG In women who have a malignant form of GTD, hCG concentrations stay the same (plateau) or they rise. Persistent elevation of serum hCG levels after a non molar pregnancy (normal term pregnancy, or preterm pregnancy, or abortion) always indicate persistent GTD.Women with persistent abnormal vaginal bleeding after any pregnancy, and women developing acute respiratory or neurological symptoms after any pregnancy, should also undergo hCG testing, because these may be signs of undiagnosed GTD (2).Women with a hydatidiform mole have an excellent prognosis and those with a malignant form of GTD usually have a very good prognosis.Choriocarcinoma is an uncommon, yet it is curable cancer, although it's highly malignant tumour and a life threatening disease, it is very sensitive to chemotherapy. All women with non-metastatic disease are cured the prognosis is good for those with metastatic disease in the early stage .Hysterectomy can be offered to patients > 40 years of age. (10)

Patients and method:

This study was a descriptive observational studyconducted from January 2008 until January 2014 in Babylon Maternity and Paediatrics Teaching Hospital ,all cases with molar pregnancy been involved, signed consent to be registered at the time of diagnosis, all gave full history and physical examination been performed and sent for investigations serum beta HCG, ultrasound ,chest X – ray ,complete blood picture and blood group and preparation of blood, evacuation by suction curettage and follow up the patient by beta HCG with referral of those with persistence or high HCG for chemotherapy in chemotherapy Centre in Marjan Teaching Hospital . Follow up after evacuation every other week HCG measurement until normalisation for all cases then monthly for six months .In cases of persistence trophoblastic activity and diagnosis of gestational trophoblastic neoplasia referral for chemotherapy and shared follow up with oncologist for response then monthly follow up after normalisation for twelve months.

Statistical analysis SPSS version 11 was used for statistical analysis also frequencies, percents, mean, S.D was done for some variables, Chi-square test was used fortesting association between different variables. Pvalue <0.05 was considered as statisticallysignificant.

RESULTS

Our study involved 83 patients with trophoblastic disease attended Babylon Maternity & Paediatric Teaching Hospital during six years period from January 2008 till January 2014.The overall mean age was (28.40±8.89) years old.Twenty- four patients their age below 20 years(28.9%),39 patients (47%) their age between20-35 years old and 20patients (24.1%) of patients were older than 35 years(P value 0.444) which was statistically not significant, the range of age (16 – 45) years old .There were 15 patients over the age of 40 years old, from them 14 patients had complete mole, two of them changed to persistent mole and one ended by hysterectomy, and another with invasive mole as shown in Figure (1).

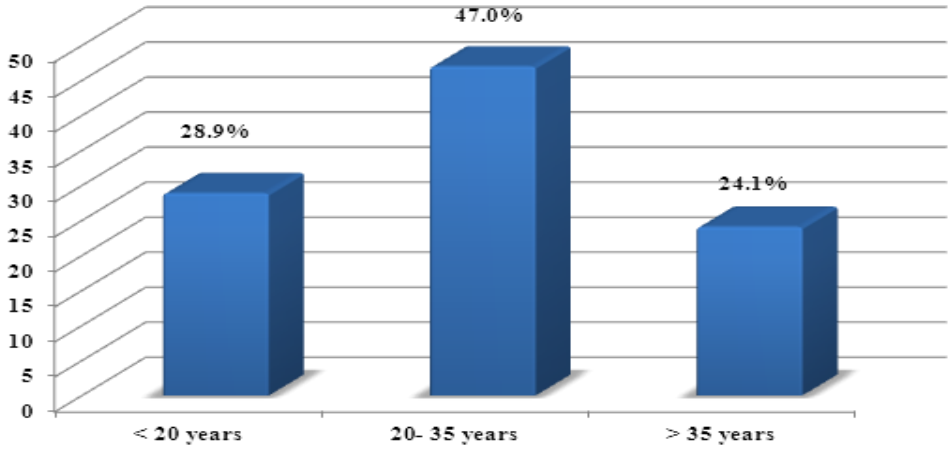

Figure -1- Distribution of patients by age groups

In our study 83 patients with trophoblastic disease 74 of them were having complete hydatidiform mole (89.2%), four patients (4.8%) having partial mole, four patients with invasive mole (4.8%) and one patient with choriocarcinoma (1.2%) as shown in Figure 2.

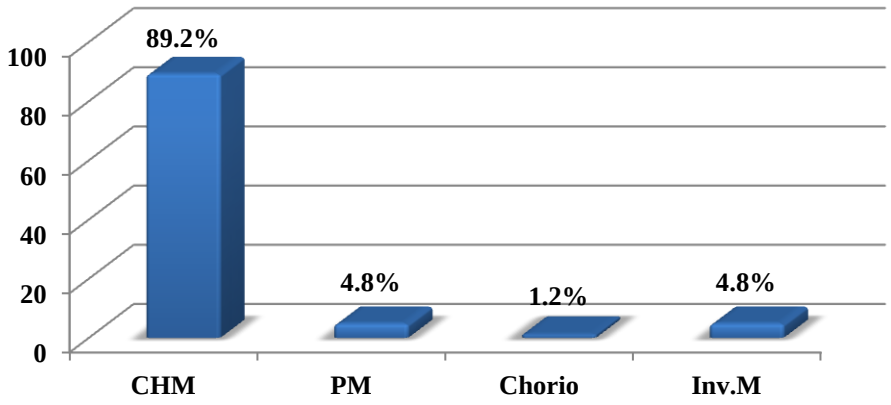

Figure 2: Distribution of patients by type of trophoblastic disease

Regarding parity ranged from(0 – 8)para,28 patients (33.8%) their parity were less than three, meanwhile 55 patients (66.3%) their parity more than three P value (0.978) which was statistically not significant, as shown in Figure (3), twenty five patients with complete hydatidiform mole their parity were between 0- 3 forming (33.8%) and 49 patients their parity were more than three forming (66.2%)**.**Patients with partial mole (4)their parity less than three, those with invasive mole three of them their parity more than three and one less than three. One case of choriocarcinoma she's Para eight.

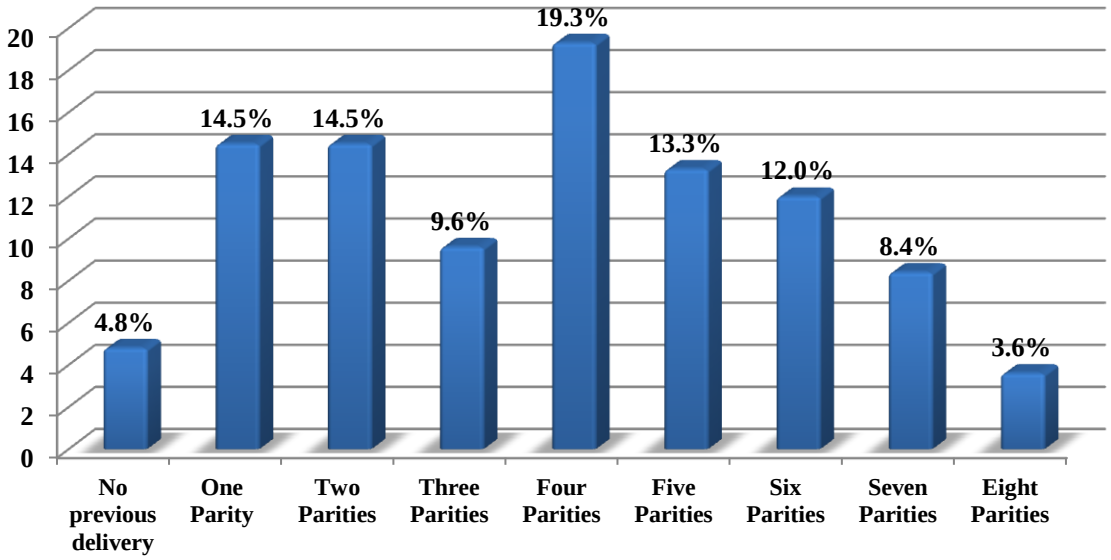

Figure 3: Distribution of patients by number of parity

About patient's residence in our study 56 patients (67.5%) were from rural area, meanwhile, 27 patients (32.5%) were from urban area P value (0.118) which was statistically not significant as shown in Figure 4.

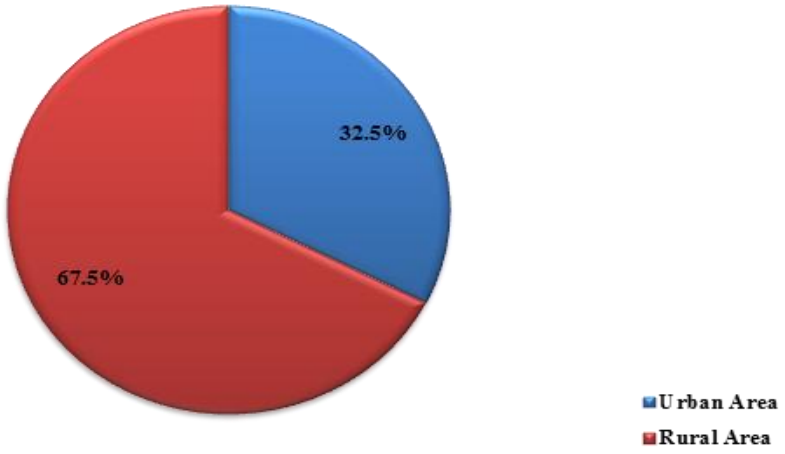

Figure 4: Distribution of patients by residence

In our study, 83 women with trophoblastic disease six of them ended by hysterectomy(7.2%), 74 women with complete hydatidiform mole suction curettage performed for them only one patient, she is 45 years Para 8 with complete mole hysterectomy done for her for heavy bleeding during the procedure of the evacuation. 11 (8.14%) out of 74 patients complete hydatidiform moles developed gestational trophoblastic neoplasia necessity chemotherapy for persistent high hCG, four patients with partial mole treated by suction curettage and four patients with invasive mole and one case choriocarcinoma ended with hysterectomy performed for them followed by chemotherapy. Those five cases in which hysterectomy performed for them, one after multiple pregnancy with hydatidiform mole after eight weeks from abortion and suction curettage continued high HCG started chemotherapy still heavy bleeding and high hCG ended by hysterectomy which revealed invasive mole and another one continued high HCG with multi-agent chemotherapy after suction curettage then hysterectomy revealed invasive mole in one part within the myometrium, the third case of hysterectomy due to persistent bleeding one year after the evacuation and high hCG, then continued after hysterectomy with multi-agent chemotherapy been well, the fourth case presented with hypo-volemic shock nine weeks from term delivery emergency hysterectomy performed revealed choriocarcinoma . The fifth case was invasion within the myometrium and the cervix and high hCG nine weeks following suction curettage and heavy bleeding.

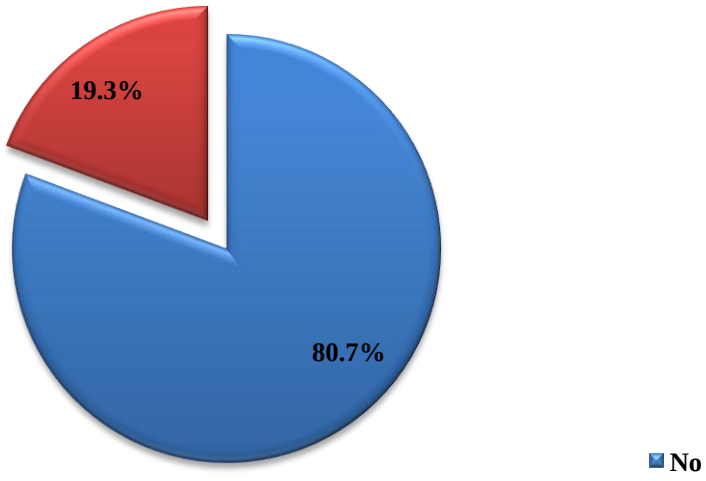

Figure 5: Distribution of patients by method of treatment

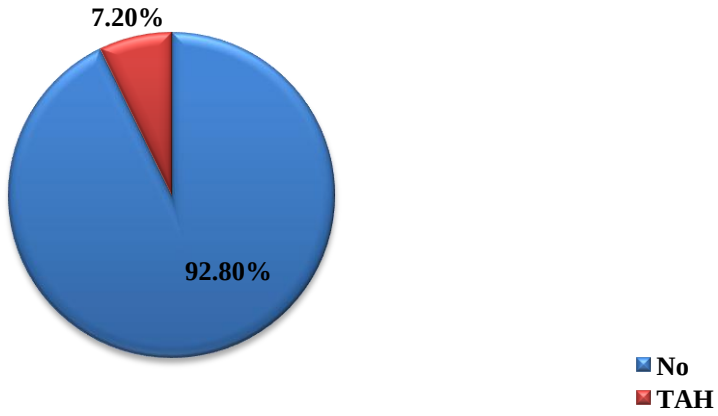

Figure 6: Distribution of patients by taking chemotherapy

Table 1: Mean difference of HCG by trophoplastic disease

*p value ≤ 0.05 is significant

Trophoplastic disease	N	Mean ± SD	t-test	P value
CHM	74	29540.54 ± 26151.13	1.091	0.278
Other	9	39833.33 ± 31431.47		

Regarding B-hCG levels pre-evacuation in our study for complete hydatidiform mole mean (29540+-26151)mIU/ml, for partial mole more than 20000mIU/ml, for invasive mole more than 30000 mIU/ml and for choriocarcinoma more than 100000 mIU/ml.

Regarding chemotherapy 16 patients (19.3%) out of 83 received chemotherapy eleven after complete hydatidiform mole for persistent high hCG forming (8.14%),four patients with invasive mole and one case choriocarcinoma, while 67 patients (80.7%) did not received any chemotherapy which was statistically significant P value (0.003) as in Figure (6).

DISCUSSION

In our study the range of age (16 – 45) years old, mean age was (28.40±8.89) years old and (24.1%) of patients were older than 35 years. Women with complete hydatidiform mole older than women with partial mole and more liable for persistent trophoblastic activity .We found that 23 patients (27.7%) their age under 20 years old and 15 patients over the age of 40 (18%), of which 14 had complete mole, of these two of them changed to persistent mole and one ended by hysterectomy, and another with invasive mole. Researchers have also found that, at the onset and end of the reproductive age, the incidence of hydatiform mole will increase to double compare to all reproductive ages (11). Maternal reproductive age is the most consistent risk factor for GTD in every region and ethnic group which was seen in our study and also in a study done by Rozina (12), who stated that the disease was more common at extremes of reproductive ages. This is also consistentwith the findings of studies from Singapore, Karachi and Nawabshah.(13)

Regarding type of trophoblastic disease in our study 83 patients with trophoblastic disease 74 of them were having complete hydatidiform mole (89.2%), four patients (4.8%) having partial mole, four patients with invasive mole (4.8%) , one patient with choriocarcinoma (1.2%) ,and no patient with placental site tumour. In a retrospective study of 112 patients, approximately 70% had a hydatiform mole and 30% were diagnosed with choriocarcinoma.Of these, only 20% of the patients were over age 35 and the average age was 28.5 years (14).Another study by Carton, etal, more than 80% of hydatiform moles are benign. In 10-15% of cases, hydatiform moles may develop into invasive moles (15) which was toour findings..Khairunnisa (2009) found that the Hydatidiform mole was diagnosed in 21(70%) patients,invasive mole in 7 (23.3%) and choriocarcinomain 2 (6.6%) patients. No patient had placental site trophoblastic tumour (16).Chhabra and Qureshi, 2007 stated that out of 99 cases of the gestational trophoplastic neoplasm (GTN) managed in 10 years, there were 88.88% cases of hydatidiform mole, 8.08% of partial mole and 3.03% of invasive(17). WhileChawla, 2006 confirmed that Partial mole constitutes 15-25% of the molar pregnancies (18). In other study the incidence of complete mole percentage is (80%), partial mole (18.4 %) and invasive mole is (1.6 %) (19). the results were similar to the result of the above mentioned authors. No patient had placental site trophoblastic tumour.

Regarding parity in our study ranged from (0 – 8), 28 (33.8%) their parity less than three and 55 (66.3%) their parity more than three which was statistically not significant.InAltieri and

Moodleystudies,hydatidiform mole pregnancy was seen moreamong nulliparous women, (19, 20) while in theKabouze, (21) Nowak(22) and pang (23)studies,hydatidiform mole incidence among multiparouswomen was more. In Harma study there was notclear correlation between parity andhydatidiform mole incidence (24).

About patient's residence in our study 56 (67.5%) were from rural area and 27(32.5%) from urban area there was no statistical significance. Nutritional and socioeconomic factors appear to be important risk factors for molar pregnancy in some populations. (25) Another study conducted byTham stated that the high incidence in Asia isgenerally attributed to low socioeconomic statusand malnutrition. (26)

Regarding B-hCG levels pre-evacuation in our study we stated for complete hydatidiform mole more than 20000 mIU/ml, for partial mole more than 20000mIU/ml, for invasive mole more than 30000 mIU/ml and for choriocarcinoma more than 100000 mIU/ml. Al-Alaf and Ibrahim Omer 2010 stated that B-hCG level in partial mole was less than 2000 mIU/ml, in complete mole was more than 10000 mIU/ml and in invasive was more than 10000 mIU/ml.(27)Furthermore Muller and Cole (2008) confirmed that hydatidiform mole often presents with much higher hCG levels and can reach > 10000 mIU/ml (28). Another study by Zahraa (2013) found the highest level of B-hCG in partial mole is up to 4000 mIU/ml, and in complete mole is 10000 mIU/ml and more, and in invasive mole is more than 10000 mIU/ml.(29)

Regarding chemotherapy 16 patients (19.3%) out of 83 received chemotherapy eleven after complete hydatidiform mole for persistent high hCG forming (14.9%), four patients with invasive mole and one case choriocarcinoma. From a study by RaziehMohammad,etal 108 Patients who presented with complete moles, 37 (34.2%) progressed into persistent moles.(30)

In our study, 83 women with trophoblastic disease six of them ended by hysterectomy(7.2%), 74 women with complete hydatidiform mole suction curettage performed for them only one patient, she is 45 years Para 8 with complete mole hysterectomy done for her for heavy bleeding during the procedure of the evacuation. a study shows that primary hysterectomy does not worsen the prognosis of gestational trophoblastic disease(31).The other five cases in which hysterectomy performed for them, one for choriocarcinoma and state of heavy bleeding forty- two days from term delivery, the other four cases for invasive mole. However, these figures may under represent the true incidence of the disease because of problemswith reporting. GTN may develop after a molar pregnancy, a non-molar pregnancy or a live birth. The incidence after a live birth is estimated at 1/50 000. (2)

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