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# Original Research Article Effect of Pre Evacuation Serum B hCG Levels on Post Evacuation B hCG Regression in Molar Pregnancy

Authors

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## ABSTRACT

**Background:** Gestational trophoblastic disease encompasses several disease processes that originate in the placenta. Before 1969, metastatic choriocarcinoma was almost invariably fatal, whereas most patients are now cured and usually retain reproductive function. The basis for this dramatic change is earlier diagnosis, the ability to precisely measure human chorionic gonadotropin (hCG), and the availability of effective chemotherapy the cure rate is greater than 90% even in the presence of widespread metastasis<sup>[11]</sup>. Precise follow-up of patients and precise monitoring using a reliable assay of hCG are essential to good results.

Aim of the study: was to study the effect of pre evacuation Serum  $\beta$  hCG levels on the post evacuation regression of  $\beta$  hCG levels in molar pregnancy.

**Methodology:** This study was conducted for period of 1 year at a tertiary care center Sree Avittom Thirunal Hospital, Government Medical College, Trivandrum, a cohort of patients who attended the vesicular mole clinic following evacuation of molar pregnancy where recruited.

Statistical tests used are mean, SD, Percentage, chi square and Odds Ratio to assess association of the selected parameters with delayed regression of serum  $\beta$  hCG levels in molar pregnancy.

**Results:** *Of the 95 patients who met the inclusion criteria and recruited in this study of 28 were late regressers* of  $\beta$  hCG included as cases and 67 were controls. Maximum number of cases in this study were in the age group of 20-30 years. Both the cases and controls were comparable with respect to age.(X2 = 0.821 P= 0.663) No significant association. In this study majority of the patients were Hindus.  $(X^2=0.136 P=0.934)$ No statistically significant association was obtained with religion on  $\beta$  hCG regression. Majority of patients In this study belonged to low socio-economic status,  $(X^2=4.135 P=0.04)$  low socio-economic status was found to be statistically significant. Blood group was not found to be an important factor affecting  $\beta$  hCG regression  $(X^2=0.503 P=0.918)$ . In this study, 60.7% of cases were Primi gravidas and among controls 55.2% were Primi gravidas. Previous conception was not found to be statistically significant.  $(X^2=3.166 P=0.367)$ . Period of gestation was not found to be an important factor affecting  $\beta$  hCG regression. (X<sup>2</sup>=0.778 P=0.477) Uterine size statistically significant effect on  $\beta$  hCG regression. In this study, 78.6% cases and only 34.3% controls had uterine size >POA. Odds ratio calculated was 7.014 CI=2.494 to 19.727 and  $X^2$ =15.505 P=0.00. 32.1% of cases had moderate proliferation and 14.9% of controls had moderate proliferation.  $X^2=2.476$  P=0.29 Effect of trophoblastic proliferation was not found to be statistically significant. 50% cases had theca lutein cysts when compared to 26.9% of controls.  $X^2$ =4.731 P=0.028 OR=2.722 CI=1.088 to 6.809. Presence of theca luetin cyst was found to be statistically significant.82.1% of cases in this study had complete moles, when compared to 56.7% of controls,  $X^2$ =5.55 P=0.015 OR=3.511 CI=1.191 to 10.394 found to be statistically significant. In this

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study, 50% cases had  $\beta$  hCG >40,000 while only 20.9% controls had the same. This was found to be statistically significant,  $X^2$ =8.047 P=0.05, Odds ratio was 3.78 CI=1.5 to 9.7. Level of pre-evacuation  $\beta$  hCG had Statistically significant effect on  $\beta$  hCG regression.

**Conclusion:** Gestational trophoblastic neoplasia (GTN) is a highly curable group of pregnancy related tumours; approximately 50% of cases of GTN arise from molar pregnancy. The serial quantitative measurement of hCG is essential for the diagnosis, monitoring the efficacy of treatment, and follow -up of patients to detect a neoplastic change at the earliest.

**Keywords-** *Gestational trophoblastic disease, Partial molar pregnancy, Complete molar pregnancy, human chorionic gonadotropin (hCG).* 

## Introduction

Gestational trophoblastic disease encompasses several disease processes that originate in the placenta. These include complete and partial moles, placental site trophoblastic tumours, choriocarcinomas, and invasive moles.<sup>[2]</sup> HM, or pregnancy, results from abnormal molar fertilization of the oocyte (egg). It results in an abnormal foetus. The placenta grows normally with little or no growth of the fetal tissue. The placental tissue forms a mass in the uterus. On ultrasound this mass often has a grape-like appearance, as it contains many small cysts which is described as snow storm appearance.

- Partial molar pregnancy. There is an abnormal placenta and some fetal development.
- Complete molar pregnancy. There is an abnormal placenta and no fetus.

Chance of mole formation is higher in older women. A history of mole in earlier years is also a risk factor.

Symptoms of a molar pregnancy may include: Abnormal growth of the uterus, either bigger or smaller than usual, severe nausea and vomiting, Vaginal bleeding during the first 3 months of pregnancy. Symptoms of hyperthyroidism, including heat intolerance, loose stools, rapid heart rate, restlessness or nervousness, warm and moist skin, trembling hands, or unexplained weight loss

Symptoms similar to preeclampsia that occur in the first trimester or early second trimester, including high blood pressure and swelling in the feet, ankles, and legs (this is almost always a sign of a hydatidiform mole, because preeclampsia is extremely rare this early in a normal pregnancy). A hydatidiform mole is considered malignant if metastases or destructive invasion of the myometrium (i.e., invasive mole) occurs, or when the serum hCG levels plateau or rise during the period of follow-up and an intervening pregnancy is excluded. Malignancy is diagnosed in 15-20% of patients with a complete hydatidiform mole and 2-3% of partial moles. <sup>[5,6]</sup> Lung metastases are found in 4-5% of patients with a complete hydatidiform mole and rarely in cases of partial hydatidiform moles <sup>[7,8]</sup>.

Certain studies have suggested a higher incidence of GTD in Asia than in North America or Europe. A review published in the American Journal of Obstetrics and Gynaecology in 2010 indicates that choriocarinoma, a subset of GTN, affects 1 in 40,000 pregnancies in Europe and North America versus 9.2 in 40,000 pregnancies in Southeast Asia and Japan.<sup>[1]</sup> A seminar in The Lancet in 2010 estimated choriocarcinoma to occur in 1 in 5 0.000 deliveries in the UK.<sup>[3]</sup> The same seminar found that placental site trophoblastic tumor accounted for about 0.2% of cases of gestational trophoblastic disease in the UK in 2010.Four clinicopathologic conditions make up this entity: 1) invasive mole (IM) that follows either a complete (CHM) or partial hydatidiformmole (PHM),2) choriocarcinoma (CCA), 3) placental site trophoblastic tumor (PSTT) and 4) epithelioid trophoblastic tumor (ETT). Each of these conditions can perforate the uterine wall. metastasize and lead to death if left untreated. Approximately 50% of cases of GTN arise from molar pregnancy, 25% from miscarriage or tubal pregnancy, and 25% from term or preterm pregnancy. Invasive mole and choriocarcinoma,

which make up the vast majority of these tumours, always produce substantial amounts of human chorionic gonadotropin (hCG) and are highly responsive to chemotherapy with an overall cure rate exceeding 90%, making it usually possible to achieve cure while preserving fertility.<sup>[4]</sup> This success is due to the unique sensitivity of these two trophoblastic neoplasms to chemotherapy and the use of hCG as a tumour marker for diagnosis, monitoring treatment and follow-up. In contrast, PSTT and ETT, which rarely occur, produce scant amounts of hCG and are relatively resistant to chemotherapy.<sup>[3]</sup>

The serial quantitative measurement of hCG is essential for the diagnosis, monitoring the efficacy of treatment, and follow -up of patients with GTN. After evacuation of a molar pregnancy, hCG levels usually disappear in 8 to 10 weeks. After normal delivery or miscarriage, hCG levels undetectable within become 3- 6 weeks. Persistence of hCG levels indicate local or metastatic disease, which allows for early timely intervention. detection and During treatment, hCG response is used as a guide to determine whether to continue treatment with an agent or switch to another agent. hCG monitoring after treatment allows for identification of patients who relapse and require additional therapy.

## **Materials and Methods**

**Study Design:** Descriptive study of patients who were on regular post evacuation follow up at 8 weeks.

**Setting:** A tertiary care setting, Department of Obstetrics and Gynaecology, Sree Avittom Thirunal Hospital, Govt. Medical College, Trivandrum, Kerala.

## Study Duration: One year

**Inclusion Criteria:** Patients who had a histopathological diagnosis of vesicular mole and were on regular follow up were included in this study. Patients were selected from the vesicular mole clinic.

**Exclusion Criteria:** Patients with incomplete follow up were excluded from the study and also

patients who were referred from local hospitals and did not have histopathological report.

**Sample Size:** During the study period of 1 year 95 who registered in the vesicular mole clinic and fulfilled the inclusion criteria were included in the study.

**Study Variables:** Includes Socio demographic variables like age, place of residence, socioeconomic status and also history of gravidity, parity, number of previous abortions, Data was also collected on the uterine size, Serum Beta hCG level at presentation and on serial measurements, transvaginal ultrasonogrphy with type of mole, adnexal mass or any co-exisisting pathology.

The data was collected using a proforma and patients were grouped into 2 categories: Cases-Late regressors of Beta hCG and Controls- who had Beta hCG regressed at 8 weeks.

Data entry was done using Microsoft excel sheet, and data analysis was done with SPSS software.

## **Observation and Results**

95 patients were recruited in this study of which 28 (29.47%) were cases (late regressors of  $\beta$  hCG and 67(70.52%) were controls.

## Fig: 1 Distribution of cases and controls



Table: 1 E	Effect of	age on	βhCG	regression
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Age	cases	controls	
<20yrs	2 (7.1%)	7 (10.4%)	
20-30yrs	24 (85.8%)	52 (77.7%)	
>30yrs	2 (7.1%)	8 (11.9%)	
Total	28 (100%)	67 (100%)	
$X^2 = 0.821 P = 0.663 Not significant.$			

In this study maximum number of cases were seen in age group 20-30 year.

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Fig: 2 Age distribution in cases and controls 100.00% 90.00% 80.00% 70.00% 60.00% cases 50.00% 40.00% controls 30.00% 20.00% 10.00% 0.00% 20-30yrs <20vrs >30vrs

Both the cases and controls were comparable with respect to age.

# **Table: 2** Effect of religion on $\beta$ hCG regression

	U	1 0	
Religion	cases	controls	
Hindu	2 0(71.4%)	50(74.6%)	
Muslim	5 (17.9%)	10 (14.9%)	
Christian	3 (10.7%)	7 (10.5%)	
Total	28 (100%)	67(100%)	
$X^2=0.136$ P=0.934 Not statistically significant.			

In this study majority of the patients were Hindus. Religion not found to be statistically significant.

**Table: 3** Effect of socio-economic status on  $\beta$  hCG regression

Religion	cases	Controls		
Low	17(60.7%)	54(80.6%)		
Middle & High	11 (39.3%)	13 (19.4%)		
Total 28 (100%) 67(100%)				
$X^{2}=4.135 P=0.04 OR=0.372 CI=0.141 to 0.982.$				

In this study, socio-economic status was found to e statistically significant.

Fig: 3 Socio economic status



Majority of patients belong to low socio-economic status

# **Table: 4** Effect of blood group on $\beta$ hCG regression

blood group	cases	controls	
А	5 (17.9%)	16 (23.9%)	
В	11 (39.3%)	23 (34.3%)	
AB	2 (7.1%)	4 (5.9%)	
0	10 (35.7%)	24 (35.9%)	
Total	28 (100%)	67(100%)	
$X^2$ =0.503 P=0.918 Not statistically significant.			

In this study, it was found that blood group was not found to be an important factor affecting regression.

Effect of previous conception on  $\beta$  hCG regression was also studied, among cases, 60.7% were Primi gravidas, and among controls 55.2% were Primi gravidas.  $X^2=3.166 P=0.367$  Previous conception was not found to affect regression. Period of gestation did not have a statistically significant effect on  $\beta$  hCG regression  $X^2=0.778 P=0.477$ 

**Table: 5** Effect of uterine size on  $\beta$  hCG regression

uterine size	Cases	controls
more than period of gestation	22 (78.6%)	24 (34.3%)
less than period of gestation	6 (21.4%)	44 (65.7%)
Total	28 (100%)	67(100%)

X<sup>2</sup>=15.505 P=0.00 OR=7.014 CI=2.494 to 19.727. Statistically significant

# Fig: 4 Uterine size and $\beta$ hCG regression



In this study, 78.6% cases and only 34.3% controls had uterine size >POA. Odds ratio calculated was 7.014.

Effect of trophoblastic proliferation on  $\beta$  hCG regression was also studied 32.1% of cases had moderate proliferation and 14.9% of controls had moderate proliferation.  $X^2=2.476 P=0.29$  Effect of trophoblastic proliferation was not found to be statistically significant.

# **Table: 6** Effect of theca lutein cyst on $\beta$ hCG regression

	Theca lutein cyst	cases	controls
	present	14 (50%)	18(26.9%)
ĺ	Absent	14 (50%)	49(73.1%)
	Total	28 (100%)	67(100%)

X<sup>2</sup>=4.731 P=0.028 OR=2.722 CI=1.088 to 6.809 statistically significant



#### Fig: 5 theca lutein cyst on $\beta$ hCG regression

In this study, 50% cases had theca lutein when compared to 26.9% controls. Presence of theca luetin cyst was found to be statistically significant.

**Table: 7** Effect of type of mole on  $\beta$  hCG regression

Type of mole	cases	controls
Complete	23 (82.1%)	38(56.7%)
Partial	5 (17.9%)	29(43.3%)
Total	28 (100%)	67(100%)

 $x^{2}=5.55$  P=0.015 OR=3.511 CI=1.191 to 10.394 Statistically significant In this study, 82.1% of cases had complete moles, when compared to 56.7% of controls, found to be statistically significant.

**Table: 8** Effect of pre-evacuation  $\beta$  hCG levels on  $\beta$  hCG regression

beta hCG level(mIU/mL)	cases	controls
> 40000	14 (50%)	14(20.9%)
< 40000	14 (50%)	53(79.1%)
Total	28 (100%)	67(100%)

 $x^2=8.047 P=0.05 OR=3.78 CI=1.5 to 9.7$  Statistically significant. In this study, 50% cases had  $\beta$  hCG >40,000 while only 20.9% controls had the same. This was found to be statistically significant.

## Discussion

Out of 95 patients recruited in this study, 28 were cases with late regression of  $\beta$  hCG at 8 weeks after evacuation of molar pregnancy and 67 who had their  $\beta$  hCG regressed were controls.

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Increasing maternal age is associated with late  $\beta$ hCG regression. In this study maximum number of cases were seen in age group 20-30 year. Both the cases and controls were comparable with respect to age.  $X^2 = 0.821 P = 0.663$  age was not found to be significant. Ahyan et al in a study found that post molar GTD was found in age group >35 yrs. Other studies also show that hydatidiform mole is more common at the extremes of reproductive age. Women in their early teenage or perimenopausal years are most at risk. [9,11,12,13] Women older than 35 years have a 2-fold increase in risk. Women older than 40 years experience a 5- to 10-fold increase in risk compared to younger women. In this study majority of the patients were Hindus. Religion not found to be statistically significant. Majority of patients in this study belonged to low socioeconomic status,  $(X^2=4.135 P=0.04)$  low socioeconomic status was found to be statistically significant. Blood group was not found to be an important factor affecting  $\beta$  hCG regression.

Hurteau JA et al has reported that clinical factors that have been associated with risk of malignant disease are advanced maternal age, high levels of hCG (>100,000 mIU/mL), eclampsia, hyperthyroiddism, and bilateral theca lutein cysts.<sup>[14]</sup> Previous conception was not found to be statistically significant.  $(X^2=3.166 P=0.367)$ . Period of gestation was not found to be an important factor affecting  $\beta$  hCG regression.  $(X^2=0.778 P=0.477)$  Uterine size Statistically significant effect on  $\beta$  hCG regression. In this study, 78.6% cases and only 34.3% controls had uterine size >POA. Odds ratio calculated was 7.014 CI=2.494 to 19.727 and  $X^2 = 15.505 P = 0.00$ . 32.1% of cases had moderate proliferation and 14.9% of controls had moderate proliferation.  $X^2 = 2.476$ *P*=0.29 Effect of trophoblastic proliferation was not found to be statistically significant. 50% cases had theca lutein cysts when compared to 26.9% of controls.  $X^2 = 4.731$ P=0.028 OR=2.722 CI=1.088 to 6.809.Presence of theca luetin cyst was found to be statistically significant.82.1% of cases in this study had complete moles, when compared to 56.7% of

controls,  $X^2=5.55 P=0.015 OR=3.511 CI=1.191$ to 10.394 found to be statistically significant. In this study, 50% cases had  $\beta$  hCG >40,000 while only 20.9% controls had the same. This was found to be statistically significant,  $X^2=8.047 P=0.05$ , Odds ratio was 3.78 CI=1.5 to 9.7. Level of preevacuation  $\beta$  hCG had Statistically significant effect on  $\beta$  hCG regression.

## Conclusion

The serial quantitative measurement of hCG is essential for the diagnosis, monitoring the efficacy of treatment, and follow -up of patients with GTN. After evacuation of a molar pregnancy, hCG levels usually disappear in 8 to 10 weeks. After normal delivery or miscarriage, hCG levels become undetectable within 3 - 6 weeks. Persistence of hCG levels indicate local or metastatic disease, which allows for early detection and timely intervention.

## Recommendation

Because of early diagnosis and appropriate treatment, the current mortality rate from hydatidiform mole is essentially zero. Approximately 20% of women with a complete mole develop a trophoblastic malignancy. Careful assessment and follow up of patients is essential to detect a malignant change at the earliest, so strict adherence to protocol is mandatory.

## References

- 1. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol 2010;203(6):531–9.
- Schorge JO, Goldstein DP, Bernstein MR, Berkowitz RS. Recent advances in gestational trophoblastic disease. J Reprod Med. 2000 Sep. 45(9):692-700.
- 3. Seckl MJ. Gestational trophoblastic disease. The Lancet 2010; 376(9742):717-29.
- 4. Berkowitz RS, Goldstein DP. Current management of gestational trophoblastic

diseases. Gynecol Oncol. 2009; 112:654–662.

- Lurain JR, Brewer JI, Torok EE, Halpern B. Natural history of hydatidiform mole after primary evacuation. Am J Obstet Gynecol. 1983 Mar 1. 145(5):591-5.
- Goto S, Yamada A, Ishizuka T, Tomoda Y. Development of postmolar trophoblastic disease after partial molar pregnancy. Gynecol Oncol. 1993 Feb. 48(2):165-70.
- Cheung AN, Khoo US, Lai CY, et al. Metastatic trophoblastic disease after an initial diagnosis of partial hydatidiform mole: genotyping and chromosome in situ hybridization analysis. Cancer. 2004 Apr 1. 100(7):1411-7.
- Menczer J, Girtler O, Zajdel L, Glezerman M. Metastatic trophoblastic disease following partial hydatidiform mole: case report and literature review. Gynecol Oncol. 1999 Aug. 74(2):304-7.
- Grimes DA. Epidemiology of gestational trophoblastic disease. Am J Obstet Gynecol. 1984 Oct 1. 150(3):309-18.
- Jeffers MD, O'Dwyer P, Curran B, Leader M, Gillan JE. Partial hydatidiform mole: a common but underdiagnosed condition. A 3-year retrospective clinicopathological and DNA flow cytometric analysis. Int J Gynecol Pathol. 1993 Oct. 12(4):315-23.
- Palmer JR. Advances in the epidemiology of gestational trophoblastic disease. J Reprod Med. 1994 Mar. 39(3):155-62.
- 12. Bandy LC, Clarke-Pearson DL, Hammond CB. Malignant potential of gestational trophoblastic disease at the extreme ages of reproductive life. Obstet Gynecol. 1984 Sep. 64(3):395-9.
- Bracken MB. Incidence and aetiology of hydatidiform mole: an epidemiological review. Br J Obstet Gynaecol. 1987 Dec. 94(12):1123-35.
- 14. Hurteau JA. Gestational trophoblastic disease: management of hydatidiform

mole. Clin Obstet Gynecol. 2003 Sep. 46(3):557-69.

- Amir SM, Osathanondh R, Berkowitz RS, Goldstein DP. Human chorionic gonadotropin and thyroid function in patients with hydatidiform mole. *Am J Obstet Gynecol.* 1984 Nov 15. 150(6):723-8.
- 16. Sun SY, Melamed A, Joseph NT, et al. Clinical presentation of complete hydatidiform mole and partial hydatidiform mole at a regional trophoblastic disease center in the United States over the past 2 decades. *Int J Gynecol Cancer*. 2015 Nov 19.
- Berkowitz RS, Goldstein DP, Bernstein MR. Natural history of partial molar pregnancy. *Obstet Gynecol.* 1985 Nov. 66(5):677-81.
- Fishman DA, Padilla LA, Keh P, Cohen L, Frederiksen M, Lurain JR. Management of twin pregnancies consisting of a complete hydatidiform mole and normal fetus. *Obstet Gynecol.* 1998 Apr. 91(4):546-50.
- 19. Steller MA, Genest DR, Bernstein MR, Lage JM, Goldstein DP, Berkowitz RS. Natural history of twin pregnancy with complete hydatidiform mole and coexisting fetus. *Obstet Gynecol.* 1994 Jan. 83(1):35-42.
- 20. Florio P, Severi FM, Cobellis L, et al. Serum activin A and inhibin A. New clinical markers for hydatidiform mole. *Cancer*. 2002 May 15. 94(10):2618-22.
- Fulop V, Mok SC, Berkowitz RS. Molecular biology of gestational trophoblastic neoplasia: a review. *J Reprod Med.* 2004 Jun. 49(6):415-22.