Original Research Article

Effect of Pre Evacuation Serum \( \beta \) hCG Levels on Post Evacuation \( \beta \) 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 with cure rates greater than 90% even in the presence of widespread metastasis\(^[1]\). 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 regressors 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.\( (X^2 =0.821 P=0.663)\) 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. 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. \( (X^2 =0.778 P=0.477)\) 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 \( X^2 =15.505 P=0.00\). Theca lutein 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 β 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 β hCG had Statistically significant effect on β 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.[2] HM, or molar pregnancy, results from abnormal 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. [5,6] Lung metastases are found in 4-5% of patients with a complete hydatidiform mole and rarely in cases of partial hydatidiform moles [7,8].

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 choriocarcinoma, 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. A seminar in The Lancet in 2010 estimated choriocarcinoma to occur in 1 in 5 0,000 deliveries in the UK. [3] 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 hydatidiform mole (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. 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.

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. 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 ultrasonography with type of mole, adnexal mass or any co-existing 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 β hCG and 67 (70.52%) were controls.

Fig: 1 Distribution of cases and controls

Table: 1 Effect of age on β hCG regression

<table>
<thead>
<tr>
<th>Age</th>
<th>cases</th>
<th>controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20yrs</td>
<td>2 (7.1%)</td>
<td>7 (10.4%)</td>
</tr>
<tr>
<td>20-30yrs</td>
<td>24 (85.8%)</td>
<td>52 (77.7%)</td>
</tr>
<tr>
<td>&gt;30yrs</td>
<td>2 (7.1%)</td>
<td>8 (11.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (100%)</td>
<td>67 (100%)</td>
</tr>
</tbody>
</table>

X² =0.821 P=0.663 Not significant.

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.

Table: 2 Effect of religion on β hCG regression

<table>
<thead>
<tr>
<th>Religion</th>
<th>cases</th>
<th>controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hindu</td>
<td>2 (71.4%)</td>
<td>50 (74.6%)</td>
</tr>
<tr>
<td>Muslim</td>
<td>5 (17.9%)</td>
<td>10 (14.9%)</td>
</tr>
<tr>
<td>Christian</td>
<td>3 (10.7%)</td>
<td>7 (10.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (100%)</td>
<td>67 (100%)</td>
</tr>
</tbody>
</table>

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 β hCG regression

<table>
<thead>
<tr>
<th>Religion</th>
<th>cases</th>
<th>controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>17 (60.7%)</td>
<td>54 (80.6%)</td>
</tr>
<tr>
<td>Middle &amp; High</td>
<td>11 (39.3%)</td>
<td>13 (19.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (100%)</td>
<td>67 (100%)</td>
</tr>
</tbody>
</table>

X^2 = 4.135 P = 0.04 OR = 3.72 CI = 1.41 to 9.985.

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

Fig: 3 Socio-economic status

Majority of patients belong to low socio-economic status.

Table: 4 Effect of blood group on β hCG regression

<table>
<thead>
<tr>
<th>blood group</th>
<th>cases</th>
<th>controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>5 (17.9%)</td>
<td>16 (23.9%)</td>
</tr>
<tr>
<td>B</td>
<td>11 (39.3%)</td>
<td>23 (34.3%)</td>
</tr>
<tr>
<td>AB</td>
<td>2 (7.1%)</td>
<td>4 (5.9%)</td>
</tr>
<tr>
<td>O</td>
<td>10 (35.7%)</td>
<td>24 (35.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (100%)</td>
<td>67 (100%)</td>
</tr>
</tbody>
</table>

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 β 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 β hCG regression X^2 = 0.778 P = 0.477.

Table: 5 Effect of uterine size on β hCG regression

Table: 5 Effect of uterine size on β hCG regression

<table>
<thead>
<tr>
<th>uterine size</th>
<th>cases</th>
<th>controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than period of gestation</td>
<td>22 (78.6%)</td>
<td>24 (34.3%)</td>
</tr>
<tr>
<td>less than period of gestation</td>
<td>6 (21.4%)</td>
<td>44 (65.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (100%)</td>
<td>67 (100%)</td>
</tr>
</tbody>
</table>

X^2 = 15.505 P = 0.00 OR = 7.014 CI = 2.494 to 19.727. Statistically significant

Fig: 4 Uterine size and β 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 β 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.
Increasing maternal age is associated with late β 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 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 β 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, hyperthyroidism, and bilateral theca lutein cysts.[14] 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 β hCG regression. ($X^2 = 0.778 \ P = 0.477$) Uterine size Statistically significant effect on β 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. $X^2 = 4.731 \ P = 0.028 \ OR=2.722 \ CI=1.088 \ to \ 6.809$ statistically significant.
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 pre-evacuation \(\beta\) 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**

14. Hurteau JA. Gestational trophoblastic disease: management of hydatidiform


