

# MAGNITUDE OF GESTATIONAL TROPHOBLASTIC DISEASE AT HAWASSA UNIVERSITY COMPREHENSIVE SPECIALIZED HOSPITAL, ETHIOPIA: A FIVE-YEAR RETROSPECTIVE ANALYSIS

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## ABSTRACT

**BACKGROUND:** Gestational Trophoblastic Disease (GTD) is a spectrum of interrelated conditions but histologically distinct disease entities originating from placenta. It can be associated with significant morbidity and mortality in the absence of timely and proper intervention.

**OBJECTIVE:** The main objective of this study was to assess magnitude of gestational Trophoblastic diseases and associated factors in Hawassa University Comprehensive Specialized Hospital.

**METHODS:** A retrospective review was conducted in Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia from September 11, 2005 to September 11, 2010.E.C. The medical records of patients managed for GTD and the total number of deliveries during the study period were retrieved. There was a total of 16,957 deliveries and 194 Gestational trophoblastic cases. The data were entered with Epi data version 3.1statistical software and exported to Statistical Package for Social Sciences version 22.0 for analysis

**RESULTS:** The magnitude of gestational trophoblastic disease was 11.4%. Gestational trophoblastic disease deliveries were diagnosed in the first pregnancy 15.5% of cases and 40.2% between para one and four. Vaginal bleeding was the most common presenting symptom 87.1% and 46.4% patients had anemia at admission and 26.3% of patients were transfused with blood. Hydatidiform mole was the commonest disease accounting for 90.2%. Suction curettage was the commonest treatment modality 70.8%. Having history of GTD, hyperemesis gravidarum, respiratory symptoms and not referred cases had a statistically significant association with hydatidiform mole

**CONCLUSION:** The burden of Gestational Trophoblastic Disease is high in the hospital.

**KEYWORDS:** Gestational trophoblastic disease, molar pregnancy, hydatidiform mole, choriocarcinoma, Ethiopia

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## INTRODUCTION

Gestational trophoblastic disease (GTD) refers to a spectrum of interrelated conditions but histologically distinct disease entities originating from placenta<sup>1</sup>. It usually occurs during conception and changes the process and outcome of pregnancy by developing abnormal fertilization and placenta<sup>2</sup>. It could happen months or years after any antecedent pregnancy that the lady encountered. It encompasses a spectrum of interrelated tumors and includes complete and partial hydatidiform mole, placental site trophoblastic tumor, and choriocarcinoma, which have varying propensities for local invasion and metastasis<sup>1</sup>. Although persistent trophoblastic tumors (GTTs) most commonly follow a molar pregnancy, they can occur after any gestational event, including induced or spontaneous abortion, ectopic pregnancy or term pregnancy<sup>3,4</sup>. These diseases are characterized by a reliable tumor marker,  $\beta$ -subunit of human chorionic gonadotropin ( $\chi$  hCG) which is important for follow up<sup>5</sup>.

Its incidence has been reported differently in various geographic areas and among different target population. It showed a decreasing trend in the developed world while still remain to be a significant problem in developing countries<sup>6</sup>. The incidence of molar pregnancies in the united states is 1 per 1000 pregnancies, in the United kingdom 1.5 per 1000, and in Japan 2 per 1000. In Nigeria, incidences of 3.8 per 1000 deliveries in the northeast while 4.7 per 1000 deliveries in southeast<sup>3</sup>. The major well-established risk factors for GTD are advanced maternal age and a past history of GTD but the exact etiology is not known<sup>7</sup>.

It affects women's health during her pregnancy and rest of her life. It even could be a cause of maternal mortality<sup>8</sup>. It induces uterine bleeding and as a result makes the mothers to be anemic and suffer from its consequences. Also, it is likely that the mother experience hyperemesis gravidarum, preeclampsia, hyperthyroidism, symptoms of lung function shortage and acute abdominal manifestations<sup>9,10</sup>. The most common presentation of patient with GTD is vaginal bleeding and other symptoms include abdominal swelling, pain, excessive vomiting and passage of vesicles<sup>3,7,11</sup>.

Suction curettage is optimal method of evacuation regardless of uterine size, in patients who have a desire of child bearing, because it carries a significantly lower risk of excessive bleeding, infection and retained molar tissue than methods involving induction (with oxytocin or prostaglandins). Patients who have completed their families or don't wish to retain reproductive function may undergo hysterectomy<sup>12</sup>. Prophylactic chemotherapy is considered to be particularly useful in the management of patients with high risk molar pregnancy (initial serum  $\beta$ -hCG more than 100,000 mIU/ mL, uterine size larger than dates, theca lutein cysts more than 6 cm in diameter, maternal age over 40) specially when hormonal follow up is either unavailable or unreliable<sup>13</sup>. Patients diagnosed to have GTD need regular follow up after suction evacuation and or hysterectomy. But most studies indicate that this follow up is poor, for example it is only 23.3% in Nigeria<sup>14-16</sup>. The incidence of the disease is believed to vary with racial and environmental factors approximately 0.5-5 per 1000 deliveries or 0.23-12.9 per 1000 pregnancies<sup>6</sup>. In some of societies, high range incidence of molar pregnancies is assigned to nutrition and socio-economic factors. It showed a decreasing trend in developed world; while still remain to be a significant problem in developing countries like Ethiopia. In our set up its magnitude, clinical presentation, treatment outcomes and follow up after management is not known.

## METHODS:

### Study area and period

The study was conducted in Hawassa university comprehensive specialized hospital, which is one of the teaching hospitals in the whole country, Hawassa town. Hawassa is located at 270 km to south east of the capital city of Ethiopia, Addis Ababa. Hawassa university comprehensive specialized hospital is the first referral hospital established in the region serving as a teaching hospital for the College of Medicine and Health Science of Hawassa University, with a catchment population of 10-12 million. It serves about 43,384 patients of all types per year. It was conducted from July 8, 2010 to November 6, 2011 E.C.

### **Study design**

A retrospective document review of GTD patients managed at Hawassa university comprehensive specialized hospital

### **Source population**

The source population was all pregnant mothers who were admitted to obstetrics and gynecologic unit of Hawassa university comprehensive specialized hospital from September 11, 2005 to September 11, 2010.E.C

### **Study population**

The study population was all pregnant mothers admitted to obstetric and gynecologic unit of Hawassa university comprehensive specialized hospital with diagnosis of GTD during the study period.

### **Inclusion criteria**

All clinical diagnosed GTD patients during the study period.

### **Exclusion criteria**

Those cases with suspected GTD but their diagnosis changed after management. Women whose charts were lost or grossly incomplete were excluded from the study

Sample size and sampling technique  
Based on the inclusion and exclusion criteria of the study, all cases managed for Gestational trophoblastic disease 194 patients' chart were retrieved and reviewed during the study period.

### **Data collection instrument**

Data were collected from patient's chart after medical record number was obtained from log-books of the Gynecology OPD, Gynecology ward and major operation room. Finally, medical records from patients' card were entered into a structured check list by trained medical interns. The check list was pretested and all questionnaires form was checked for completeness and accuracy. Any problem encountered during the data collection was reported to principal investigator for immediate action

### **Operational definitions**

Anemia: hemoglobin level of <11g/d in the 1st trimester and <10.5g/d in the 2nd trimester.

Gestational trophoblastic disease: a pregnant woman with vaginal bleeding with or without passage of vesicles and ultrasound features of molar pregnancy and or confirmed histologically. Asymptomatic cases

with incidental finding by ultrasound based on clinical diagnosis.

### **Data Processing and Analysis**

The collected data was checked visually by the investigators, then data was coded, entered and cleaned using Epi-Data version 3.1 software and finally exported into SPSS version 22 for analysis. Descriptive statistical analysis such as simple frequencies, measures of central tendency and measures of variability was used to describe the characteristics of participants. Then the information was presented using frequencies, summary measures, tables, and figures (charts). Bivariate analysis, COR with 95% CI, was used to see the association between each independent variable and the outcome variable by using binary logistic regression. AOR with 95% CI was estimated to identify the factors associated with outcome variable using multivariable logistic regression analysis. Level of statistical significance was declared at  $p\text{-value} \leq 0.05$

### **Data quality assurance**

During data collection, the principal investigator checked the completeness, ambiguous suspicions and checked on the spot. Before feeding the information into the computer, it was checked for completeness and accuracy

### **Ethical consideration**

Ethical clearance was obtained from Institutional Review Board (IRB) of College of Medicine and Health Sciences, Hawassa University and no personal identifiers was collected. Confidentiality was maintained during data collection, analysis and interpretation.

## **RESULTS**

### **Socio-demographic characteristics**

In five years, period there were a total of 16,957 deliveries, with 203 Gestational trophoblastic disease cases, 194 cases were eligible for analysis and 9 cases were excluded from the study due to failure to meet the inclusion criteria. The age of the patients ranged from 16-50 years with a mean ( $\pm$  1SD) of 30.8 ( $\pm$  8.6) years. More than half of patients (56.2%) came from greater than 50 km distance and 62(32%) of patients came from >100 km. Out of these cases 135(69.6%) came with referral paper (Table 1)

**Table 1: Socio-demographic characteristics of women with GTD admitted at HUSCH, Southern Ethiopia from September 11, 2005 to September 11, 2010 E.C**

Variables	Category	Frequency	Percent
Age in years	<=20	26	13.4
	21-30	91	46.9
	31-40	52	26.8
	41-50	25	12.9
Distance from health facilit	<50 km	85	43.8
	50-100 km	47	24.2
	>100 km	62	32
Region	SNNP	83	42.8
	Oromia	111	57.2
Referred case	Yes	135	69.6
	No	59	30.4

GTD was diagnosed in the nulliparous women in 30(15.5%) cases. Most of them (n=74, 40.2%) were para 1 to 4. Seven (3.6%) patients had history of previous GTD while 33(17%) and 4(2.1%) had history of previous abortion and ectopic pregnancy respectively. Majority of patients with GTD, 90(46.4%) were diagnosed during second trimester, 80(41.2%) during first trimester whereas 9(4.6%) were in the third trimester. Menstrual history was documented for 101(52.1%) of cases and out of these 72(71.3%) have had regular menses while 29(28.7%) have had irregular menses. (Table 2)

**Table 2: Reproductive History and Gestational age of women with GTD admitted at HUCSH, Southern Ethiopia from September 11, 2005 to September 11, 2010**

Variables	Category	No. of cases	Percentage
History of previous abortion	Yes	33	17
	No	161	83
History of previous GTD	Yes	7	3.6
	No	187	96.4
History of previous Ectopic pregnancy	Yes	4	2.1
	No	190	97.9
Parity status	Nulliparous	30	15.5
	1-4	78	40.2
	5-8	63	32.5
	9 and above	23	11.9
Gestational age in week	≤12week	80	41.2
	13-20 week	90	46.4
	>20week	9	4.6
	Unknown GA	15	7.7

## Magnitude of GTD

The magnitude of GTD was 1.14 % (194 of 16,957) deliveries and 7.8/1000 deliveries and 2.5/1000 deliveries for complete and partial hydatidiform mole respectively, 0.5/1000 deliveries for invasive mole, 0.6/1000 deliveries for choriocarcinoma and there was no patient with a diagnosis of placental site trophoblastic tumor. The highest prevalence of GTD varies from year to year, 1.57% (62 of 3957) in the year of 2008 E.C and lowest (0.73%) was in 2006 E.C, (20 cases among 2723) deliveries.

Clinical presentation and management of patients with gestational trophoblastic disease

Patients had variable presenting complaints. Vaginal bleeding was the most common (n=169, 87.1%) presenting symptom followed by abdominal pain and large for date uterus in 73(37.6%) of cases for each (Table 3)

**Table 3. Clinical presentation cases with Gestational trophoblastic disease (n=194) admitted at Hawassa University Compressive Specialized Hospital, Southern Ethiopia from September 11, 2005 to September 11, 2010 E.C**

Variables	Number of cases	Percentage
Vaginal bleeding	169	87.1
Passage of vesicles	59	30.4
Big for date uterus	73	37.6
Abdominal pain	73	37.6
Respiratory symptoms	23	11.9
Theca-lutein cyst size > 6cm	19	9.8

Anemia was a common (n=90, 46.4%) medical complication, hyperthyroidism in 55(28.4%) and preeclampsia in 34(17.5%) of cases, Twelve (6.2) and 11 (5.7%) patients had shock and respiratory distress, respectively. Theca-lutein cysts were found in 19(9.8%) of patients.

Most of patients were managed by suction curettage, 136(70.8%) while 56(56/194=28.9%) patients were managed by total abdominal hysterectomy (TAH). TAH with bilateral salpingo-oophorectomy (BSO) was done for 2 cases and TAH with unilateral salpingo-

ophorectomy(USO) for 5 cases). Fifty-one (26.3%) of patients were transfused with blood. Four patients were treated with methotrexate.

Factors associated with hydatidiform mole

In the bivariate analysis, absence of the following conditions: previous history of GTD, passage of vesicles, respiratory symptoms, theca luiten cyst, anemia, hyperemesis gravidarum, shock, respiratory

embarrassment and not referred patient as well as absence of blood transfusion were identified to be associated with hydatidiform mole. However, in multiple logistic regression analysis, only absence of previous history of GTD, absence of respiratory symptoms, absence of hyperemesis gravidarum and not referred patient remained significantly associated with hydatidiform mole ( $P < 0.05$ ) (Table 4)

**Table 4: Bivariate and multivariate logistic regression analysis showing factors associated with hydatidiform mole patients admitted at Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia from September 11, 2005 to September 11, 2010 E.C**

Variables	Hydatidiform mole(n=194)		COR (95% C.I)	AOR (95% C.I)
	Yes (N=175)	No'(n=19)		
Previous history of GTD				
Yes	3	4	1	1
No	172	15	15.2(3.13-7.77)*	5.40(5.50-4.6) *
Passage of vesicles				
Yes	50	9	1	1
No	125	10	2.25(0.86-5.87)	1.70(0.44-6.59)
Respiratory symptom				
Yes	14	9	1	1
No	165	10	10.3(3.61-29.67)*	16.89(3.73-76.58) *
Theca leutin cyst				
Yes	15	4	1	1
No	160	15	2.84(0.54-9.67)	3.63(0.66-19.70)
Anima				
Yes	77	13	1	1
No	98	6	2.76(1.0-7.59) *	1.67(0.29-9.70)
Hyperemesis gravidarum				
Yes	12	3	1	1
No	163	16	2.55(0.65-9.98)	8.06(1.20-5.4) *
Shock				
Yes	9	3	1	1
NO	166	16	3.46(0.85-14.08)	1.60(0.16-15.58)
Respiratory embarrassment				
Yes	7	4	1	1
No	168	15	6.40(1.68-24.37)	0.96(0.12-7.40)
Patient referred				
Yes	118	17	1	1
No	57	2	4.11(0.92-18.4)	5.95(1.02-4.84) *
Blood transfusion				
Yes	40	11	1	1
No	135	8	4.64(1.74-12.3) *	1.86(0.37-9.40)

\*P value <0.05

## DISCUSSION

The magnitude of gestational trophoblastic disease in this study was 11.4 per 1000 deliveries, that is 7.8/1000 deliveries and 2.5/1000 deliveries for complete and partial hydatidiform mole respectively, 0.5/1000 deliveries for invasive mole, 0.6/1000 deliveries for choriocarcinoma and there was no patient with a diagnosis of placental site trophoblastic tumor. It is in line with study in Egypt 6.6/1000 deliveries<sup>12</sup>, 7.2/1000 deliveries in Nigeria<sup>17</sup>, done lower than study done in Turkey, 12.1 per 1000 deliveries<sup>7</sup> and it is higher than other study done in Saudi Arabia 0.9/1000<sup>18</sup>, 1.1/1000 deliveries in Uganda<sup>19</sup> and 2.8/1000 deliveries in two teaching hospitals in Ethiopia<sup>6</sup>. This discrepancy might be due to difference in health care systems to manage and early detection of Gestational trophoblastic disease and it might be due to socio economic and cultural difference.

This study showed that the diagnosis of GTD was made during second trimester for majority of patients which similar with study done in Uganda<sup>19</sup>. In contrary to the result of other study showed that majority were diagnosed during first trimester<sup>9,15,19</sup>. This is may be due to most of our patients are not evaluated with routine first trimester ultrasound after history amenorrhea which can identify the problem, even though they may be asymptomatic at the time of diagnosis. It could also be due to access to health care limitation.

This study has also demonstrated that almost all the cases reviewed were diagnosed clinically and the diagnosis was confirmed using histopathologically for few cases. This data is in contrary to other studies which demonstrated that clinical diagnosis was confirmed with histopathological for most cases<sup>3,5,12,15,18</sup>. In this finding vaginal bleeding was the commonest presenting symptom which is similar with other study<sup>2-18</sup>. The finding of this study confirmed that anemia was the commonest complication which account 46.4% cases followed by hyperthyroidism 28.4% and preeclampsia 17.5% Which is similar with others findings<sup>3,15,19</sup>. In this study complete mole was commonest types of GTD which accounted 68% of cases which was similar to other studies<sup>7,15,19</sup>.

## CONCLUSION

The findings showed that the burden of Gestational Trophoblastic Disease is persistently high in the study facility. Moreover, majority of patients presented to Hawassa hospital was late.

## LIMITATIONS OF THE STUDY

Since the study was retrospective, details of socio-demographic factors, obstetrics characteristics, management follow up and final treatment outcome was not assessed in detailed. The incidence of subsequent pregnancies after complete treatment of GTD was not studied.

## DECLARATIONS

Ethical approval and consent to participant  
Ethical clearance was obtained from Institutional Review Board (IRB) of College of Medicine and Health Sciences, Hawassa University. Confidentiality was maintained during data collection, analysis and interpretation

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## AVAILABILITY OF DATA AND MATERIAL

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

## CONSENT FOR PUBLICATION

Not applicable

## COMPETING INTERESTS

The authors declare that they have no competing interests.

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