

# Gestational trophoblastic diseases in a teaching hospital in northern, Nigeria

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**Abstract:** Background: Gestational trophoblastic diseases (GTD) is a spectrum of pregnancy-related premalignant disorders of complete and partial hydatidiform mole, and the malignant disorders of invasive mole, choriocarcinoma, and the rare placental-site trophoblastic tumour. Objective: This study was carried out to determine the incidence of gestational trophoblastic disease, the clinical features and management outcome at the Aminu Kano Teaching Hospital, Kano, Nigeria. Materials and Methods: This was a retrospective study of the demographic and clinical data as well as management outcome of all patients with gestational trophoblastic disease managed between January, 2008 and December, 2012 at the Aminu Kano Teaching Hospital, Kano, Nigeria. Results: There were 103 cases of GTD and 22,680 deliveries; giving an incidence of GTD as 4.5 per 1000 deliveries. Among them, 69 (67.0%) cases were hydatidiform mole while Choriocarcinoma was diagnosed in 34 cases (33.0%). The antecedent pregnancy among the cases of choriocarcinoma were hydatidiform mole in 18 cases (52.9%), miscarriage in 10 cases (29.4%) and ectopic pregnancy in 1 case (3.0%) and full term pregnancy in 5 (14.7%) patients. GTD was commoner at the extremes of reproductive age. Hydatidiform mole was high 37 (53.6%) in those aged 24 years and below, while choriocarcinoma was high 13 (38.2%) in 45 - 49 years age group. The most common presenting symptom was vaginal bleeding occurring in all the cases, while anaemia was the most common complication. Suction evacuation and follow up (67.0%) was the mode of treatment in all cases of molar pregnancy. Only cases of choriocarcinoma 34 (33.0%) had chemotherapy, 11 (32.4%) cases had single agent while 23 cases (67.6%) had multi-agent chemotherapy. There were seven maternal deaths in this study, given a case fatality of 6.8%. Conclusion: The incidence of GTD in this study was 4.5 per 1000 deliveries. Vaginal bleeding was the commonest presenting symptom. Early diagnosis and appropriate treatment of this disease has an excellent prognosis, while late presentation was associated with high maternal mortality as found in this study.

**Keywords:** Molar Pregnancy, Choriocarcinoma, Maternal Mortality

## 1. Introduction

Gestational trophoblastic disease (GTD) encompasses a range of pregnancy related disorders, consisting of the premalignant disorders of complete and partial hydatidiform mole, and the malignant disorders of invasive mole, choriocarcinoma, and the rare placental-site trophoblastic tumour<sup>1</sup>. These malignant forms are termed gestational trophoblastic neoplasia (GTN)<sup>1</sup>. Although GTN typically follows a molar pregnancy, they can occur after any gestational event<sup>2,3</sup>.

The incidence of GTD varies in different regions of the world. 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<sup>2,3,4</sup>. In Nigeria, incidences of 3.8 per 1000 and 4.7 per 1000 deliveries were reported from Northeast and Southeast respectively<sup>5,6</sup>. In general, areas with high incidence of molar pregnancies have proportionately greater incidence of choriocarcinoma arising from hydatidiform mole<sup>4</sup>.

The aetiology of gestational trophoblastic disease is not well understood. However, hydatidiform moles affect women throughout the reproductive age range but are more common at the extremes of the range<sup>7</sup>. Women under 16 have a six times higher risk of developing the disease than those aged 16-40, and women who conceive aged 50 years or more have a one in three chance of having a molar pregnancy<sup>7</sup>. There is higher incidence in women of Far Eastern origin and Africa than for white women from the United Kingdom and other

Western countries<sup>7,8</sup>. The reasons for this are not clear but might reflect low socioeconomic status and diet deficient in protein, folic acid and carotene<sup>4,6,8</sup>.

Patients with hydatidiform mole usually present with amenorrhoea, vaginal bleeding and spontaneous passage of grape-like vesicles. There may also be hyperemesis gravidarum. Examination may reveal a doughy uterus which may be large for the gestational age. There may be adnexal masses as a result of bilateral theca lutein cyst and rarely, they may present with features of thyrotoxicosis and pre-eclampsia in the first half of pregnancy<sup>9</sup>. High serum and urinary  $\beta$  human chorionic gonadotrophin ( $\beta$ -hCG) levels are characteristics of the disease. However, ultrasonography which shows classic "snowstorm" appearance is a reliable and sensitive technique for a pre-evacuation diagnosis but the definitive diagnosis is made by histological examination of the products of conception<sup>8</sup>. The clinical course is defined by the patient's serum  $\beta$ -hCG curve after evacuation of the mole<sup>9,10</sup>. In 80% of patients with hydatidiform mole, serum  $\beta$ -hCG levels steadily drop to normal within 8-12 weeks after evacuation of the molar pregnancy<sup>9,10</sup>. However, women who have the malignant form of GTD may show  $\beta$ -hCG titres, which either plateau or rise and remain elevated beyond 8 weeks<sup>11</sup>. New pregnancy and/or presence of other tumours like non gestational choriocarcinoma, embryonal cancer and polyembryomas that secrete  $\beta$ -hCG for example, could confuse management<sup>4</sup>.

Gestational trophoblastic neoplasia (invasive mole or choriocarcinoma) follows complete mole in 15-20% of cases and less than 5% of partial moles will develop post molar GTN<sup>4,12</sup>. The World Health Organisation has proposed prognostic risk scoring system which reliably assesses the potential for resistance to chemotherapy<sup>4,7</sup>. Score < 7 represents low risk of resistance to chemotherapy while score  $\geq 7$  represents high risk<sup>8,12,13</sup>. GTD are generally highly responsive to chemotherapy<sup>11</sup>. However, hysterectomy remains an option for good surgical candidates not desirous of future pregnancy, women who are older and more likely to develop malignant sequelae, presence of placenta site trophoblastic tumour and cases complicated by haemorrhage<sup>9</sup>. Hysterectomy does not eliminate the need for careful follow up with  $\beta$ -hCG testing, although the likelihood of metastatic disease following hysterectomy for GTD decreases from 20% to 3 - 5%<sup>8,13</sup>. Early stage GTN disease is often cured with single-agent chemotherapy<sup>14,15</sup>. In contrast, advanced stage disease requires multi-agent combination chemotherapeutic regimens to achieve a cure<sup>7,14,15</sup>. GTD is one of the few highly curable human tumors, even in the setting of advanced disease and widespread metastases.

This study was carried out to determine the incidence of gestational trophoblastic disease, the clinical features and management outcome at the Aminu Kano Teaching Hospital, Kano, Nigeria.

## 2. Materials and Methods

This was a retrospective descriptive study carried out at

the Aminu Kano Teaching Hospital, Kano Nigeria. Kano is in the Northern part of Nigeria where the tribe was mostly hausas. The case records of all the patients with gestational trophoblastic disease managed between January, 2008 and December, 2012 were retrieved. The outcome measures were the socio-demographic characteristics of the patients, clinical presentation, modalities of treatment, management outcome, complications, and follow up. The data obtained were analyzed using SPSS, and presented in tabular form using frequencies and percentages, mean and standard deviation..

## 3. Results

There were 103 cases of GTD out of 4,529 gynaecological admissions during the study period, there by constituting 2.3% to total gynaecological admissions. There were 22,680 deliveries; hence the incidence of GTD was 4.5 per 1000 deliveries. Of 103 cases of GTD, 69(66.9%) were hydatidiform mole and 34 (33.1%) were choriocarcinoma.

The age range of the patients was 15 - 59 with a mean of  $37 \pm 5$  years. GTD was commoner at the extremes of reproductive age. Hydatidiform mole was high 37(53.6%) in those aged 24 years and below, while choriocarcinoma was high 13(38.2%) in 45 - 49 years age group.

**Table 1.** Age Distribution and Type of GTD

Age range	H.Mole	Choriocarcinoma
	Frequency (%)	Frequency (%)
15 - 19	21(30.4)	-----
20 - 24	16 (23.2)	4 (11.8 )
25 - 29	7 (10.1 )	4(11.8 )
30 - 34	5 (7.2)	1(2.9)
35 - 39	3 (4.3)	1(2.9)
40 - 44	6(8.7)	3(8.8)
45 - 49	8(11.6)	13(38.2)
50 - 54	2(2.9)	7 (20.6)
55 - 59	1(1.4)	1 (2.9)
TOTAL	69(100)	34(100)

**Table 2.** Parity Distribution of GTD

Parity	Frequency	Percentage
0-1	39	37.9
2-3	20	19.4
4 - 5	18	17.5
>5	26	25.2
TOTAL	103	100

**Table 3.** Ethnic Distribution of Patients

Ethnic group	Frequency	Percentage
Hausa	60	58.3
Igbo	11	10.7
Fulani	13	12.5
Yoruba	5	4.9
Others	14	13.6
TOTAL	103	100

**Table 4.** Clinical Presentation of Patients

Symptoms	Frequency	Percentage
Vaginal bleeding	103	100
Abdominal swelling	52	50.5
Excessive vomiting	40	38.8
Lower abdominal pain	20	19.4
Passage of vesicles	11	10.7
Cough	7	6.8
Dyspnoea	5	4.9

Majority of the patients 60(58.3%) were Hausas, 11(10.7%) were Igbos while 5(4.9%) were Yorubas. The most common presenting symptom was vaginal bleeding occurring in all the cases, while anaemia defined as haemoglobin <10 g/dl was the most common complication. The antecedent pregnancy among the cases of choriocarcinoma were hydatidiform mole in 18 cases (52.9%), miscarriage in 10 cases (29.4%) and ectopic pregnancy in 1 case (3.0%) and full term pregnancy in 5(14.7%) patients. Suction evacuation and follow up (67.0%) was the mode of treatment in all cases of molar pregnancy only. Only the cases of choriocarcinoma (33.0%) had chemotherapy and follow up, 11 cases (32.4%) had single agent (Methotrexate), while 23 cases (67.6%) had multi-agent chemotherapy using Methotrexate, Actinomycin-D, and Cyclophosphamide (MAC). Twenty four patients (23.3%) had regular follow up, 52(50.5%) were irregular and 27(26.2%) did not turn up. There were seven maternal deaths in this study, given a case fatality of 6.8%.

## 4. Discussion

The prevalence of GTD in this study was 4.5 per 1000 deliveries. This is comparable to 4.7 per 1000 deliveries in Nnewi and 3.58 per 1000 deliveries in Abakaliki from Southeast Nigeria<sup>6,16</sup>. However, It is much higher than incidences of 1 per 1000, 1.3 per 1000, and 2 per 1000 pregnancies reported in the United States, the United Kingdom and Japan respectively<sup>3,8,23</sup>. The reason for low prevalence in industrialized countries compared to developing countries may be due to differences in the denominators (per pregnancies versus per deliveries) and most studies in developing countries were hospital based<sup>17</sup>.

Majority 69(66.9%) of GTD were hydatidiform mole which was similar to other studies<sup>4,16,17,23</sup>. GTD was commoner at the extremes of reproductive age. Hydatidiform mole was high 37(53.6%) in those aged 24 years and below, while choriocarcinoma was high 13(38.2%) in 45 - 49 years age group. The reason for this difference is not clear but Bugti QA et al. and Obiechina NJA et al. noted similar trend<sup>18,19</sup>. This study did not find significant statistical difference in prevalence of GTD among the three major ethnic groups (Hausa, Igbo and Yoruba) in Nigeria. However, this is an institutional study with a small sample size and may not be a good representative of the whole nation. As such, establishment of GTD central registry across the country will help to resolve this issue. The most common presenting symptom was vaginal bleeding occurring in all

the cases. This was noted in other studies<sup>6,16</sup>. Anaemia defined as haemoglobin level <10 g/dl was the most common complication and same had been reported by Ocheke et al.<sup>9</sup> and Mbamara SU et al<sup>6</sup>. This may not be unrelated to late presentation, persistent vaginal bleeding and effects of chemotherapy. Suction evacuation (67.0%) was the commonest form of treatment offered to those with GTD in AKTH. This method is currently advocated because it allows rapid evacuation of the uterus, provides specimen for histology and reduces the chance of trophoblastic tissue embolisation<sup>6,20,21</sup>. Follow-up of the patients was carried out by clinical examination, serum  $\beta$ -hCG level, and 3 monthly chest X- ray in persistent cases. Initial, follow up was carried out weekly till the  $\beta$ -hCG level was not detectable followed by monthly monitoring for 6-24 months. Chemotherapy was indicated in cases of persistent rise or plateau of  $\beta$ -hCG and in cases of choriocarcinoma. Patients with nonmetastatic (stage I) and low-risk metastatic (stages II and III, score <7) GTN were treated with single-agent methotrexate, while those with high-risk metastatic GTN (stage IV and stages II-III score  $\geq 7$ ) were treated initially with multi-agent chemotherapy. Suction evacuation and follow up (67.0%) was the mode of treatment in all cases of molar pregnancy only. Only the cases of choriocarcinoma (33.0%) had chemotherapy and follow up; 11 cases (32.4%) had single agent (Methotrexate), while 23 cases (67.6%) had multi-agent chemotherapy using Methotrexate, Actinomycin-D, and Cyclophosphamide (MAC). The high rate of post molar GTN in this study was because most cases managed were referred, from other hospital either with histology result of choriocarcinoma or on account of persistent high  $\beta$ -hCG and/or vaginal bleeding following suction evacuation. Twenty four patients (23.3%) had regular follow up, 52(50.5%) were irregular and 27(26.2%) did not turn up for follow up. This poor follow up may be as a result of poverty, cultural attitudes and inadequate health education. There were seven maternal deaths in this study, given a case fatality of 6.8% which was higher than 3.3% and 0.8% from Pakistan and Argentina respectively<sup>17,22</sup>, but much lower than similar studies in Nigeria<sup>2,6,16</sup>. This high rate of mortality in this study may be due to late presentation and inadequate treatment because of poor follow up.

## 5. Conclusion

The incidence of GTD in this study was 4.5 per 1000 deliveries. Vaginal bleeding was the commonest presenting symptom. Early diagnosis and appropriate treatment of this disease has an excellent prognosis, while late presentation was associated with high maternal mortality as found in this study.

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