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A 6-Year Review of Gestational Trophoblastic Disease in the Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Gestational Trophoblastic Disease (GTD) refers to a spectrum of diseases characterised by aberrant growth and development of the trophoblasts of the placenta that may continue even after the end of pregnancy.
Objective: To determine the prevalence, risk factors, clinical presentations and management of gestational trophoblastic disease in the Niger Delta University Teaching Hospital (NDUTH), Okolobiri, Bayelsa state, Nigeria .
Methodology: In this retrospective, descriptive, cross sectional study design, cases managed for gestational trophoblastic disease between January 2012 and December 2017 were audited using a self-developed proforma. Data collected include sociodemographic information, obstetric history, antenatal care in the index pregnancy, risk factors, management and outcome (morbidity and mortality) associated with gestational trophoblastic disease (GTD) in the Centre.
Results: There were 3172 deliveries that occurred during the 6year period under review in NDUTH with a total of 12 cases of GTDs. Hence, GTD is seen in 3.8 per 1,000 deliveries. The mean age of women with GTD was 31±6.3 years. Half of the women (50%) were in the low socio-economic class.

The mean parity was 2 ± 1.6. The mean gestational age at presentation was 16.2 ± 5.4 weeks. All the women presented with amenorrhoea, Other presenting complaints include abnormal vaginal bleeding (83.0%) and uterine size greater than date (83.0%). Hydatidiform mole and choriocarcinoma accounted for 75.0% and 25.0% of cases, respectively. Seven (58%) of the patients had suction evacuation only for the management of hydatidiform mole, 1 patient (8.3%) had suction evacuation and chemotherapy for hydatidiform mole and subsequent persistent disease. Three (25%) of the patients had chemotherapy only for Choriocarcinoma. Ten (83.3%) of the patients were successfully treated. During the study period, 2 (17%) of the patients conceived after the treatment and had spontaneous vaginal delivery at term. Three (25%) of the patients made use of contraceptive pills during follow up. There were 2 maternal deaths due to GTD giving a case fatality rate of 6.7%.

Conclusion: GTDs though rare as shown in our study, they are however still associated with maternal mortality. This study underscores the need for histo-pathological examination of products of uterine evacuation. Urgent and intensified advocacy is needed in terms of good general education, poverty alleviation and improved health-seeking behaviour of our women to enhance early diagnosis, prompt and adequate treatment.

Keywords: Gestational trophoblastic disease; clinical presentation; management; NDUTH.

1. INTRODUCTION

Gestational Trophoblastic Disease (GTD) refers to a spectrum of interrelated but histologically distinct tumours originating from the placenta [1-4]. These diseases are characterized by a reliable tumour marker (the β-subunit of human chorionic gonadotropin [β-hCG]) and have varying tendencies toward local invasion and spread [1,5-10]. On one end of the spectrum are the premalignant disorders of complete and partial hydatidiform mole, and at the other extreme are the malignant disorders of invasive mole, choriocarcinoma, and the rare placental-site trophoblastic tumour, termed malignant trophoblastic neoplasia [4-11].

The incidence of gestational trophoblastic disease varies considerably in different regions of the world [1-4]. The incidence of molar pregnancies in Japan is 2 per 1000 pregnancies, this is reportedly three times higher than the incidence in Europe or North America (0.6 – 1.1 per 1000 pregnancies) [2-3,4,12]. In the West African subregion, incidence rates of between 0.4 and 7.2 per 1000 deliveries have been reported in Nigeria and 0.8 per 1000 deliveries from Ghana [13,14]. In Tunisia an incidence rate of 1.3 per 1000 pregnancies has been reported [15]. The higher incidence among women of far Eastern origin and Africa as compared to those in the United kingdom and other western countries has been attributed to lower socioeconomic class of the women and a diet deficient in carotene, protein and folic acid [2,4]. The variation in incidence in different regions of the world may however also partly be due to differences between reporting hospital - based versus population - based data [3,6].

The risk factors reportedly associated with GTDs include age (age greater than 35years or less than 16 years), parity, previous unsuccessful pregnancy (e.g. spontaneous abortion), previous history of molar pregnancy, smoking, socio-economic and nutritional factors and in the case of choriocarcinoma, long term oral contraceptive usage [1,2,6,16 – 20].

Abnormal vaginal bleeding remains the most common presenting complaint and occurs in virtually all patients [3,5,15 21-24] especially in third world countries. As a consequence of abnormal vaginal bleeding anaemia may be present. About one quarter of women will present with a uterine size greater than dates. Hyperemesis gravidarum, preeclampsia, and symptomatic theca-lutein cysts are less commonly observed [3,21,22,23]. These sequelae, typically occur chiefly in patients who did not have early prenatal care and who present with a more advanced gestational age and markedly elevated serum B-hCG levels [3,24].

First-trimester diagnosis of hydatidiform mole is now common because of the routine use of transvaginal ultrasonography and prompt follow up with beta-hCG in suspected cases [2,3,24]. Although B-hCG levels are helpful, the diagnosis of molar pregnancy is frequently made sonographically [2,3,24]. However the definitive diagnosis of GTD is by histopathology [2,4].

Despite the relatively common occurrence of GTD in our environment, no current study has been done in our centre to evaluate the pattern of these diseases. This study sought to determine the incidence, predisposing factors, clinical presentations and management of gestational trophoblastic disease in the Niger Delta University Teaching Hospital (NDUTH) Okolobiri, Bayelsa State, Nigeria.

2. METHODOLOGY

2.1 Study Area

The study was carried out at the Niger Delta University Teaching Hospital (NDUTH), Bayelsa State, Nigeria. The study centre is a tertiary health institution with major roles of teaching, research and health services. The study was carried out in the Obstetrics and Gynaecology department of the hospital. The hospital is domiciled in Bayelsa state as one of the two leading referral centres for other health facilities within and outside the State.

2.2 Study Design

This study was a 6 year retrospective, descriptive study that reviewed all cases of GTD managed at the Niger Delta University Teaching Hospital, between 1st January 2012 to 31st December 2017.

2.3 Study Population

The records of all pregnant women with a diagnosis of GTD in the hospital in the 6 - year period under review was retrieved from the health information and management unit of the hospital and included in the study.

2.4 Study Instrument

A self-designed proforma was used for data collection. Data included sociodemographic characteristics (age, religion, ethnicity, marital status, educational status, occupation and spouse's educational status and occupation.) of the patients. Other information on the proforma include presenting symptoms, uterine size, ultrasound findings, *B*-hCG levels, mode of treatment, type of chemotherapy, contraceptive use, follow up evaluation and outcome of treatment.

2.5 Study Procedure

The study was carried out in 2019 after an approval from the Ethical committee of the hospital and permission from the head, health information and management systems of the hospital to review records. The labour ward and theatre registers of the hospital were perused to obtain identification numbers of pregnant women in the hospital with a diagnosis of gestational trophoblastic disease in the period under review. Case notes of identified pregnant women were thereafter retrieved from the archives and data for the study was extracted based on the study proforma.

2.6 Data Analysis

Data collected was entered into Microsoft excel spread sheet where it was cleaned and thereafter imported into statistical package for the social sciences (SPSS version 22) for analysis. Continuous variables were summarized as mean and standard deviation, and categorical variables with frequencies and percentages.

3. RESULTS

3.1 Sociodemographic Characteristics of Patients

There were 3172 deliveries in NDUTH during the period of this review, and 12 cases of gestational trophoblastic diseases were managed. Hence the incidence of GTD was 3.8 per 1000 deliveries. From the study, the age range of patients with GTD was 16 - 49 years and most (75%) occurred within 17-34years (Fig. 1). All the cases of choriocarcinoma occurred in women of ages between 17-34 years and most 20(50%) of the cases of hydatidiform mole also occurred in women aged 17-34 years (see Table 1). Half of the patients (50.0%) were of lower socio-economic class, those of middle socioeconomic class were 33.0% and 17.0% were of upper socio-economic class (Table 1).

3.2 Obstetric Features, Clinical Presentation and Complications

The median parity was 2 with a range of 0 - 5 and women who are para 3 and above accounted for 47.2% of those who presented with gestational trophoblastic disease. There were 75.0% cases of hydatidiform mole and 25.0% cases of choriocarcinoma. Table 1 shows the gestational age at presentation. From the study, more patients (50%) presented at gestational age between 14-26 weeks. Fig. 2 shows the common modes of presentation and

the complications of the disease noticed in the patients.

3.3 Treatment Modality

Seven (58%) of the patients had suction evacuation only for hydatidiform mole, 8.3% had suction evacuation and chemotherapy for hydatidiform mole and subsequent persistent disease. A quarter of the patients had chemotherapy only while one of the patients (8.3%) received only palliative care and died before definitive treatment could be instituted (Table 2).

Methotrexate only was used in 8.3% of the patients, MAC (Methotrexate, Actinomycin-D, Cyclophosphamide) was used in another 8.3% of patient and EMA-CO (etoposide, methotrexate, actinomycin-D, cyclophosphamide, oncovin) were used for 17.0% of the patients.

3.4 Outcome

The patients were properly followed up although one patient of the twelve (8.3%) was lost to follow up. A quarter of the patients made use of contraceptive pills during follow up. During the study period, 2 patients (17.0%) conceived after the treatment and had spontaneous vaginal delivery at term without any sequelae. There were 2 maternal deaths in this study, giving a case fatality rate of 16.7%. The patients who died, presented with FIGO stage 4B disease. The causes of death were organ failure due to distant metastasis and hypovolaemic shock.

Table 1. Sociodemographic characteristics and gestation age at presentation among the patients

Characteristics	Frequency N = 12	Percentage (%)
Age range (Years)		
≤ 16	1	8.3
17 – 34	9	75.0
≥ 35	2	16.7
Socio-economic status		
Lower	6	50
Middle	4	33
High	2	17
Gestational age (weeks)		
≤ 13	4	33
14 – 26	6	50
≥ 27	2	17

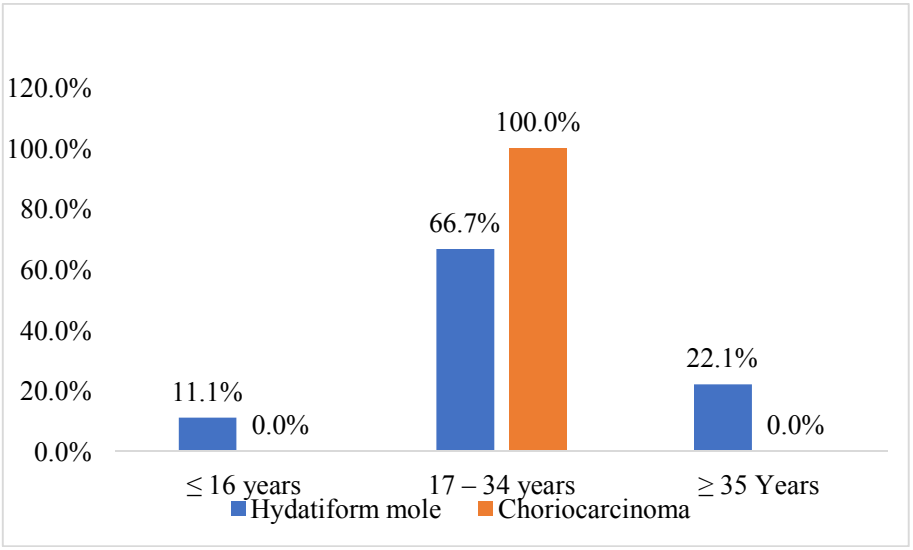

Fig. 1. Distribution of Gestational trophoblastic disease by age of patients

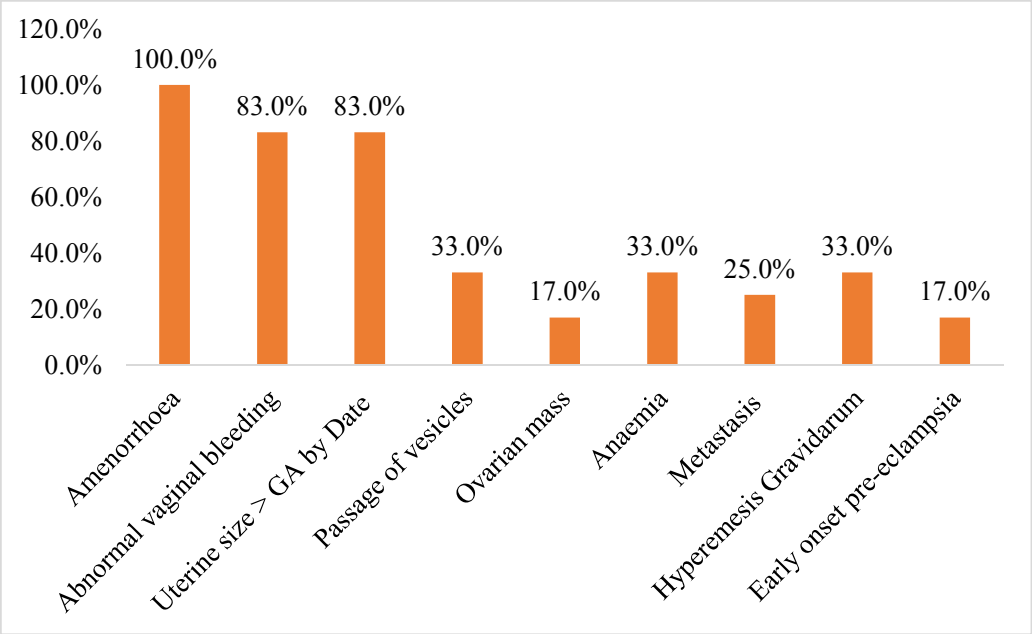

Fig. 2. Clinical Presentations/Complications noticed in the Patients. GA – Gestational Age.

Table 2. Mode of treatment

Treatment	Frequency n = 12	Percentage (%)
Chemotherapy only	3	25.0
Suction evacuation only	7	58.4
Suction evacuation + Chemotherapy	1	8.3
Palliative care only	1	8.3

4. DISCUSSION

Gestational trophoblastic tumour is of great interest because of its excellent prognosis, with the potential for childbearing maintained, if diagnosed and treated early [2-4]. The prevalence of GTD of 3.8 per 1,000 deliveries in this study was lower than that reported from other studies such as Mbamara et al in Nnewi, [25] Anuma et al. [20] in south-east Nigeria, Yakassai et al. [2] in Kano, Northern Nigeria and Bugti et al in Quetta [26] but higher than 1.3 per 1000 deliveries reported from Birmingham, England [27]. The prevalence rate of 3.8 per 1000 deliveries noted in this study was, however, similar to 1 per 332 (3.0/1000) deliveries reported from Onitsha, Southeast Nigeria [28]. The higher incidence of hydatidiform mole compared to choriocarcinoma in this study is in consonance with the findings of other studies [27,29-31]. However this finding is at variance with the study in Nnewi, south-east Nigeria [2] which has a higher incidence of choriocarcinoma compared to hydatidiform mole. The fact that most of the women with hydatidiform mole presented to us relatively early may account for this disparity as this may possibly have prevented progression to choriocarcinoma. It has already been noted above that the reporting of hospital- based versus population- based studies is a confounding factor in the comparison of the prevalence of GTD in various parts of the world [3,31]. Under-reporting, poor health seeking behaviour of our women [32], lack of a universal histopathological analysis of products of miscarriage and ectopic pregnancy and also lack of a national registry for GTD, as in Nigeria [4], makes it even more difficult for an accurate and valid comparison of the prevalence of GTD between different regions of the country and other parts of the world. Other types of GTD were not seen in this study possibly because of their relative rarity.

GTD in this study occurred mostly at the peak of the reproductive career of the women (17-34 years) and in women of low parity. This is at variance with some other studies which

demonstrated significant increase in the incidence of GTD at the extremes of reproductive ages and in women of high parity [4,27-28]. The occurrence in this study of GTD in mostly women of low parity however gives some credence to the suggestion that parity per se may not be an independent factor in the epidemiology of GTD [26,33]. Majority of the patients with choriocarcinoma were referred after suction evacuation had earlier on been carried out in a peripheral general hospital. None of the products of conception evacuated at these peripheral hospitals was sent for histopathological analysis, prior to referral by their health care providers, possibly due to lack of pathologists in such centres.

The mean gestational age at diagnosis was 16.2 weeks and this is higher than 11.5 weeks reported in Tunisia [31]. It is similar to the report from Nnewi [25]. This contrasts with the current trend in the developed world where majority of the cases are diagnosed early in pregnancy at the asymptomatic stage due to wide spread practice of routine ultrasound in early pregnancy [30,34]. Health facilities in the developed world are well equipped and better utilized by the population. In developing countries like ours, poor general education, poverty, cultural myths and poor health-seeking behaviourr, bring about late presentation of GTD [2]. Even when they present to a peripheral health facility as a result of persisting symptoms, diagnosis is delayed due to lack of appropriate skilled personnel, basic facilities and absence of a prior good index of suspicion. The relative late presentation as compared to that in developed countries could also account for the high rate of complications, among our women, as seen in this study.

Bleeding per vaginam, amenorrhoea and symphysio-fundal height more than estimated gestational age were the commonest presenting symptoms, similar to the findings in other studies [29,34].

Most of the patients had suction evacuation regardless of the size of the uterus as this is the preferred method of treatment in suspected cases of GTD [1,2,29,30]. It also provides specimen for histological analysis of the products of conception. Oxytocin infusion was commenced after some vesicles had been evacuated, as is the recommended practice, to prevent embolization of vesicles [1,5]. Chemotherapy was introduced in cases of choriocarcinoma and can also be used in cases of persistent rise or plateau of β-HCG [1,5,32]. Prophylactic use of chemotherapy has remained controversial. However prophylactic chemotherapy can be a useful option in our setting because of poor follow-up of our patients which is corroborated in other studies [20,25,28]. In some cases hysterectomy can be performed especially in women with high parity and resistant disease [35,6]. The contraception compliance in this study was also very low at 25%, but similar to findings in Nnewi [25]. The low literacy rate of the patients, ignorance, poverty, poor communication and/or inadequate health education and consequent difficulty in counselling of these patients could be contributory factors to poor outcome observed in the period under review. The case fatality rate of 16.7% seen in this study is relatively high when compared with that of other studies in Nigeria: Eniola et al at Ile-Ife(8.7%), [6]. Mbamara et al at Nnewi(13.3%), [25]. Anuma et al at Abakiliki(10%) [26] and Yakassai et al at Kano(6.8%) [2] and is very high compared with the reports of much better outcome from developed nations [6,29]. This high case fatality rate is as a result of two of the patients in this study presenting with very advanced disease(FIGO stage IVB). Relative late presentation of cases of GTD in developing countries such as Nigeria and Senegal35, as a consequence of poor education, poverty, unhealthy cultural attitudes and poor health seeking behaviour has also been noted in other similar studies2,35. Early diagnosis and adequate treatment of this condition in developed nations could explain the documented much better prognosis of this condition in their environment.

5. CONCLUSION

Though GTDs were rare in this study, hydatidiform mole was relatively more frequent as compared to choriocarcinoma and although the prognosis for complete recovery may be as high as 85 to 100%, the associated overall mortality was rather high at our centre. Early diagnosis, prompt and adequate treatment will improve the prognosis of the disease. Improved health seeking behaviour, female education/empowerment, provision of affordable diagnostic tools and a high index of suspicion, with consequent earlier diagnosis and referral at peripheral hospitals, will help reduce the complications of the disease and reduce the mortality rate. A national registry for GTD in Nigeria is urgently required.

ETHICAL APPROVAL

The study was carried out in 2019 after an approval from the Ethical committee of the hospital and permission from the head, health information and management systems of the hospital to review records.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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