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Research Article

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A Review of Gestational Trophoblastic Disease in A Tertiary Hospital in Noth-Western Nigeria

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Abstract

Background: *Gestational trophoblastic disease (GTD) encompasses a range of pregnancy related disorders of complete and partial hydatidiform mole, and the malignant disorders of invasive mole, choriorcarcinoma and the rare placental-site trophoblastic tumour.*

Aims: *The study is aimed to determine; (1) the prevalence of gestational trophoblastic tumours in Federal Medical Centre, Birnin Kebbi (2) The pattern of presentation and (3) the maternal outcome in patients with GTD managed at the Deparrtment of Obstetrics and Gynaecilogy of Federal Medical Centre, Birnin Kebbi, Nigeria.*

Methodology: *This was a retrospective study of the cases of gestational trophoblastic disease managed at the Departmenrt of Obstetrics and Gynaecology of Federal Medical Centre, Birnin Kebbi, Noth-Western, Nigeria between the 1st January, 2010 and 31st of December, 2019.*

Results: *There were 82 cases of gestational trophoblastic diseases out of 5,088 gynaecological admissions during the study period, thereby constituting 1.6% of the total gynaecological admissions. There were 16,572 deliveries; hence the incidence of GTD was 4.9 per 1000 deliveries. The age range of the patients is between 15–45years, with a mean age of 26.84 years. Of the 82-case managed during the period under review, only 74 (90.2%) of patients' case notes were retrieved for analysis. Hydatidiform mole was the commonest among them, accounted for 56.8% of cases and 6.9% of the cases were choriocarcinoma. In 50% of cases there was no documented histological diagnosis. GTD was commoner at the extremes of reproductive age.*

Conclusion: *The incidence of GTD in this study was 4.9 per 1000 deliveries. Vaginal bleeding was the commonest presenting symptom. Early diagnosis and appropriate treatment of this disease is a good determinant of the disease outcomes, while late presentation was associated with high maternal mortality as found in this study.*

Keywords: Gestational trophoblastic diseases, Tertiary health centre, Northern Nigeria.

Introduction

Gestational trophoblastic disease (GTD) refers to a spectrum of pregnancy related disorders of complete, partial hydatidform mole, through the aggressive malignancies of invasive mole, choriorcarcinoma and the rare placental-site trophoblastic tumour [1, 2]. The combination of this unique biology, relative rarity and effective therapy makes trophoblastic tumours an extremely interesting and important area of gynaecologic and oncologic care. The main types of gestational trophoblastic diseases are benign disease; the Hydatidiform (complete or partial) mole and the malignant disease of invasive mole, Choriocarcinoma, Placental-site trophoblastic tumour and Epithelioid trophoblastic tumour [3]. The malignant forms are called gestational trophoblastic neoplasia (GTN). Although the GTN typically follows a molar pregnancy, they can occur following any form of pregnancy1. These tumours are unique in that they developed from an aberrant fertilization

event and hence developed from fetal tissue within the maternal host. They are composed of both the syncythiotrophoblastic and cytotropoblastic cells, with exception of PSTT, which is derived from the intermediate trophoblastic cells [4].

The incidence of GTD varies from one region to the other. The incidence of GTD is fairly constant at approximately 1 to 2 per 1,000 deliveries in the United States, Japan and Europe [5-8]. In Nigeria, incidences of 3.8 per 1000 and 4.7 per 1000 deliveries were reported from North-East and South-East respectively [1]. In general, areas with high incidence of molar pregnancies have proportionately greater incidence of choriorcarcinoma from hydatidforrm mole [4].

The exact cause of gestational trophoblastic disease is not well understood. Hydatidiform moles affect women throughout the reproductive age range and are more common at the extremes of age [1, 11]. Women under the age of 16 years, have a six times higher risk of developing the disease than those aged 16-40, and women who conceive at age of 50 years or more have a one in three chance of having a molar pregnancy [4]. There is higher incidence in women of far Eastern origin and Africa than for white women from the United Kingdom and other Western countries [4, 11]. The reasons for this are not clear but might reflect low socioeconomic status and diet deficient in protein, folic acid and carotene [12].

Patients with hydatidiform mole usually present with amenorrhea, vaginal bleeding and spontaneous passage of grape-like vesicles. Some may also present with hyperemesis gravidarum. While patients with Choriocarcinoma may present with recurrent vaginal bleeding and anaemia following uterine evacuation due to molar pregnancy and sometimes only recurrent vaginal bleeding and ill-health following a term pregnancy. Examination may reveal a variable degree of palor, a doughy uterus which may be large for the gestational age. There may be adnexal mass (of theca lutein cyst) and rarely there may be features of thyrotoxicosis and pre-eclampsia in the first half of pregnancy [3]. High serum and urinary β human chorionic gonadotrophin levels are characteristics of the disease. However, ultrasonography which shows classic "snowstrom" appaerance is a sensitive technique and reliable for a pre-evacuation diagnosis of hydatidiform mole but the definitive diagnosis is made by histological examination of the products of conception [11]. The clinical course is defined by the patient's serum β-hCG curve after evacuation of the mole [9, 10]. In 80% of patients with hydatidiform mole, serum β-hCG levels steadily drop to normal within 8-12 weeks after evacuation of the molar pregnancy [13]. However, women who have the malignant form of GTD may show β-hCG titres, which either plateau or rise and remain elevated beyond 8 weeks [5]. New pregnancy (Hence the basis for contraception) and or presence of other tumours like non gestational choriocarcinoma, embryonal cancer and polyembryonal that secrete β-hCG for example, could confuse management [8]. Gestational trophoblastic neoplastic (invasive mole or choriocarcinoma) follows complete mole in 15-20% of cases and less than 5% of partial moles will develop post molar GTN [4, 12]. The World Health Organisation has proposed prognostic risk scoring system which assesses the potential for resistance to chemotherapy [11]. Score of < 7 represents low risk of resistance to chemotherapy while score ≥ 7 represents high risk [13]. Patients assessed to be low-risk are managed with single agent chemotherapy (Methotrexate ot actinomycin-D), though Actinomycin-D has been found to probably be more effective) [14], while those considered to be high-risk for resistance should be managed with combination therapy (EMACO or EMACE) [15]. GTDs are generally highly responsive to chemotherapy [3, 5]. 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. Hysterectomy does not eliminate the need for careful follow- up with serum β-hCG testing or any reliable marker. Although the likelihood of metastatic disease following hysterectomy for GTD decreases from 20% to 3% [4, 5]. Early stage GTN disease is often cured with single-agent chemotherapy [16]. In contrast, advanced stage disease requires multiagent combination chemotherapeutic regimens to achieve a cure [13, 16]. GTD is one of the few highly curable human tumours, even in the setting of advanced disease and widespread metastases.

Study Justification

GTD is a significant source of maternal morbidity with increased risk of mortality from complications if not detected early and treated promptly with meticulous follow up. Different institution has different management protocol, hence the need to the effectiveness of the management protocol in our facility, should there need for review.

Aim

This study is aimed to determine the prevalence, clinical presentations, diagnosis, treatment modality and outcomes of GTD in Federal Medical Centre, Birnin Kebbi, Kebbi State.

Materials Methods

This study was approved by the Human Research and Ethics Committee (HREC) of Federel Medical Centre, (FMC), Birnin-Kebbi, North-western Nigeria. This is a 10-year retrospective study of patients with GTD managed in Federel Medical Centre, (FMC), Birnin-Kebbi between 1st January, 2010 to 31st December, 2019 was undertaken. The names and hospital numbers of all the cases of GTD in the hospital over the 10 years period were obtained from the gynaecology ward, labour ward register, operating theatre registers as well as the department of Health Information Management of FMC, Birnin Kebbi. The gynaecology ward and labour ward registers also in addition provided information on the total number of gynaecological admissions and deliveries, respectively.

The variables considered included the maternal age, parity, gestational age at presentation, risk factors, clinical presentations, laboratory investigations results, modality of treatment, post-treatment

complication, treatment follow-up and treatment complications. This information was extracted from the case files obtained from the records department. The data obtained were expressed in percentages, means and standard deviations. The data processing and analysis were carried out using the Statistical Package for the Social Sciences software (SPSS) Version 20.0. Chicago.

Information obtained from the case notes were analyzed and discussed according to the said objectives, and compared with the previous studies conducted elsewhere.

Inclusion Criteria

All retrievable case files of cases of Gestational Trophoblastic Diseases managed within the stated study period were included in the study.

Exclusion Criteria

All case notes with incomplete records and those not retrieved were excluded for analysis.

Results

There were 82 cases of gestational trophoblastic disease managed at Federal Medical Centre, Birnin Kebbi within the study period. Hence, this constitutes 1.6% to total gynaecological admissions. There were 16,572 deliveries; hence the prevalence of GTD as 4.9 per 1000 deliveries. Of the 82 cases of gestational trophoblastic disease, only 74 of patients' case notes were retrieved for analysis given a retrieval rate of 90.2%. The age range of the participants was 15–45years, with a mean age of 26.8 years. However, GTD was commoner in women between the age of 30 to 34 years. Majority of the patients 60 (81.1%) were Hausas, there were 5 (6.8%) Yorubas and Igbos constitutes 4 (5.4%) of the study population. Five (6.8%) of the women belongs to the other ethnic groups. This sis shown in table 1 below Thirty (40.5%) of the women had no formal education, 8 (10.8%) had primary school level of education, 32 (43.2%) of the women had Secondary School education and only 4 patients had tertiary level of education.

Of the 74 cases reviewed, majority 42 (59.5%) of the patients presented in the second trimester, 30 (40.5%) presented in the first trimester of pregnancy, while two patients were not certain of the duration of their pregnancies.

The most common presenting symptom was vaginal bleeding which occurred in 64 (86.5%) while 10 (13.5%) had excessive vomiting. Miscarriage was the commonest antecedent pregnancy, which identified in 56 (75.7%) while 12 (16.2%) followed term pregnancies while preterm delivery was the antecedent pregnancies in 6 of the study participants. None of the patients had documented evidence of previous GTD.

Most of the patients 52 (70.3%) had normal baseline (which Liver function test, renal function test and complete blood count) laboratory parameters as well as the chest radiograph, 12 (16.2) had abnormal parameters while 10 (13.5%) had no documentation of their baseline laboratory tests. Majority 42 (56.8%) of the cases were Hydatidiform mole (of which 24 were complete mole while 18 were partial mole). Twelve (16.2%) of them were cases of choriocarcinoma, while 8 were persistent mole and placental site trophoblastic tumor (PSTT) was 2 (2.7%). Ten (13.5%) of the patients had no documented histological diagnosis.

Suction evacuation was the commonest form of treatment, which was offered to 42 patients with Hydatidform mole. Ten of the 12 patients with choriocarcinoma as well as the 8 with persistent mole received combination chemotherapy. The 2 patients who had hysterectomy due to PSTT while the remaining two of the cases of choriorcarcinoma had not received chemotherapy treatment due to late presentation and unstable clinical condition subsequently resulted in mortality.

Anaemia was the commonest 33 (44.6%) complication observed among the studied population and 13 (17.6%) of patients had recurrent vaginal bleeding while 25 (33.8%) of them had no any complication within one year of post-treatment follow-up.

Over the six months period of surveillance, 69 (95.8%) patients were on follow-up (out of which only 47 (65.3%) were regular on the follow up). Three (4.2%) of the 72 patients did not return to the clinic after treatment. However, 32 (44.4%) were not able to complete one year post treatment follow-up. Two patients died during the period given a case fatality rate of (2.7%). No mortality was documented during the follow up period.

Table 1: Socio-demographic characteristic of the patients with GTD

Age	Frequency (N)	Percentage (%)
<20	16	21.6
20-24	12	16.2
25-29	10	13.5
30-34	24	32.5
35-39	10	13.5
≥40	2	2.7
Total	**74**	**100.0**
Primigravida	18	24.3
Multigravida	37	50.0
Grandmultipara	19	25.7
Total	**74**	**100.0**
Ethnicity		
Hausa	60	86.3
Yoruba	5	6.9
Igbos	4	3.4
Others	5	3.4
Total	**74**	**100.0**

Table 2: Frequency distribution of histologic diagnosis of GTD

Histological diagnosis	Frequency	Percentage
Partial mole	18	24.3
Complete mole	24	32.4
Persistent mole	8	10.8
PSTT	2	2.7
Choriocarcinoma	12	16.2
No histology	10	13.6
Total	**74**	**100**

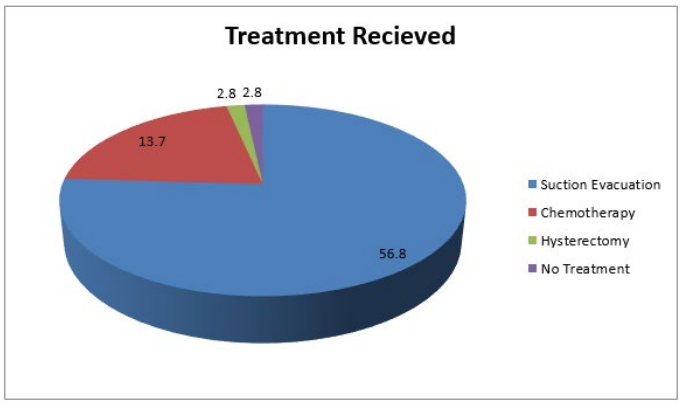

Figure 1: Patients with GTD and treatment received

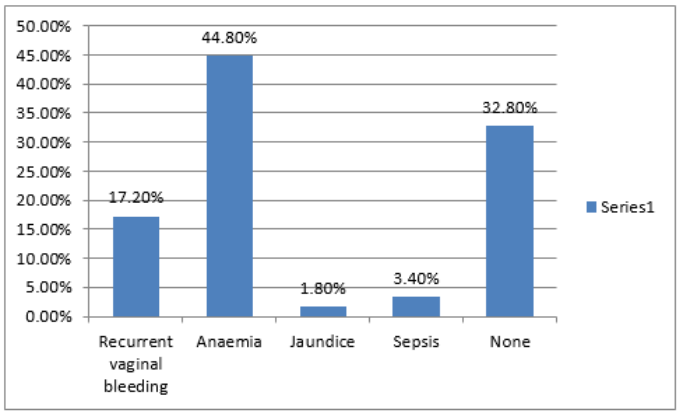

Figure 2: Main Complications of Gestational Trophoblastic Tumours

Discussion

The prevalence of GTD in this study was 4.7 per 1000 deliveries. This is comparable to 4.4 and 4.5 per 1000 deliveries reported from Abuja and Kano, Northern, Nigeria. It's also similar the 4.7 and 4.06 per 1000 deliveries in Nnewi and OnitshaA, South-estern Nigeria [1, 16, 17]. However, it is much higher than the incidences of 3.58 per 1000 deliveries from Abakaliki, South-east Nigeria and much higher than the 1-2 per 1,000 pregnancies reported in the United States, the United Kingdom and Japan [3, 18, 19]. However, it is lower than the 7.2 and 7.9 per 1000 reported from Zaria and SingaporeB [20].

The per pregnancy versus per deliveries in the developed countries could be the reason for the low prevalence in industrialized countries compared to higher prevalence in the developing countries [1]. The mean age of the patients was 26.8 years and this is similar to what was found by other studies. Hydatidiform mole constitutes 56.7% of the total cases of GTD this is higher than what was found in Nnewi, Southern Nigeria and the 30.5% and 35.3% reported from Zaria and Abuja, both of Northern Nigeria [1, 3, 16, 17, 20]. This higher incidence from our study, may be attributed to nature of our healthcare services in our centre, where our centre attend to even case ought to have been manage at the primary and secondary health facilities. However, lower than what was reported from Kano in Northern Nigeria [1]. Choriocarcinoma was high, 26 (38.2%) in 45-49 years age groups. Vaginal bleeding was the commonest presenting symptoms 86 (86.5%) and this was similar to what was reported from Kano, Nnewi, Abuja, Zari'a and Jamshoron [1, 16, 20, 21].

Fourteen (12.1%) of the patients were diagnosed co-incidently during routine ultrasound scan. About 75.0% of the patient had antecedent miscarriage and this is similar to what was reported by other studies. Suction evacuation 75.9% was the commonest form of treatment offered to those with molar gestation, regardless of the size of the uterus. This method is currently advocated in the management of molar gestation because it allows rapid evacuation of the uterus, control bleeding, provides specimen for histologic examination and reduces the chance of trophoblastic tissue embolism when compared with other methods of uterine evacuation [1, 16, 21]. Majority of the patients 86 (74.1%) in this study did not either present to the clinic after initial admission or regular on their follow-up and this is similar to what was reported from Kano by Yakasai et al. And for those that were regular to their follow-up (25.9%), were monitored by clinical examination, weekly serum β-hCG till the level was not detectable (and remission is defined as the consecutive normal β-hCG values over 2 to 3 weeks), followed by monthly monitoring for 12 months serum β-hCG level, and 3 monthly chest X- ray in persistent cases [1]. In 24 (20.7%) of cases, chemotherapy was administered, this is due to either persistent rise or plateau of the serum β-hCG and cases of choriocarcinoma. Patients with stage l (non-metastatic), and stage ll and lll (low-risk metastatic, score <7) GTN were treated with single-agent (methotrexate), while those with stage lV (high-risk metastatic score ≥7) were treated with combination chemotherapy using Methotrexate, Actinomycin-D, and Cyclophosphamide (MAC). Two patients had hysterectomy due to placenta site trophoblastic tumour (PSTT). Anaemia was the most common complication which was found in 50% of the patients and this was similar to what was reported by Yakassai et al. and Mbamara et al. [1, 16]. This may be related to late presentation of the patients, persistent or recurrent vaginal bleeding and side effects of chemotherapy (for those who had chemotherapy).

In this study, suction evacuation was done in all the cases of Hy-

datidiform mole for uterine evacuation of the molar tissue. This finding was in agreement to the Royal College of Obstetrician and Gynaecologists' practical guidelines on the management of molar pregnancy [2, 3, 23]. Suction evacuation is safe, rapid and effective in nearly all cases of Hydatidiform mole [24, 25]. In our center, as revealed by this study, over 95% of choriocarcinoma were managed by chemotherapy. Only 1 (2.4%) case had hysterectomy. Hysterectomy remains an option for good surgical candidates who are not desirous of future pregnancies, advanced age or likely tendency to develop malignant sequel in patients with HM, but none of our patients had hysterectomy due to either. This patient had hysterectomy because she had an uncontrolled haemorrhage.

There were 2 maternal deaths in this study, given a case fatality of rate 2.7% which was closer to the 3.3% reported from Pakistan19 but lower than what was reported from Kano1, Ile-Ife6, Nnewi16 and Abakaliki18. This lower mortality rate may be due to the fact that majority of cases are Hydatidiform mole and for those with malignant GTD, presents at early stage of the disease.

Conclusion

The prevalence of GTD in this study was 4.9 per 1000 deliveries. Vaginal bleeding was the commonest presenting symptom. Molar gestation was the commonest form of the GTD identified in the studied area and combination chemotherapy using EMACO was the commonest form of treatment in patient with gestational trophoblastic neoplasia.

Patient's awareness availability of funds as well as the basic facilities for diagnosis and follow up are essentially lacking in the studied area and this is so in most of the health facilities in the area.

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