Original Article

Gestational trophoblastic disease in Abuth Zaria, Nigeria: A 5-year review

Abimbola O. Kolawole, John K. Nwajagu, Adekunle O. Oguntayo, Marliya S. Zayyan, Sunday Adewuyi[1]

Departments of Obstetrics and Gynaecology, [1]Radio-Oncology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

ABSTRACT

Gestational trophoblastic diseases (GTD) includes a spectrum of diseases (tumor or tumor-like conditions) characterised by aberrant growth and development of the trophoblasts that may continue even beyond the end of pregnancy. It encompasses the benign trophoblastic disease (complete and partial moles), and the malignant trophoblastic diseases including the invasive mole (chorioadenoma destruens), choriocarcinoma, and Placental Site Trophoblastic Tumor (PSTT). This study was to determine the prevalence, risk factors, clinical presentation, diagnosis, treatment options and outcomes of GTD in Ahmadu Bello University Teaching Hospital (ABUTH) Zaria. A five-year retrospective study of patients with GTD managed at ABUTH, North-west Nigeria, from 1st January 2008 to 31st December, 2012 was undertaken. Data of all cases of GTD in the hospital over the 5 year period were obtained. The gynaecology ward and labour ward registers also provided information on the total number of gynaecological admissions and deliveries respectively. The data processing and analysis were carried out using the SPSS software version 16. The data obtained were expressed in percentages, means, and standard deviations. During the period of study there were 8,138 deliveries and 2,453 gynaecological admissions. There were 59 cases of GTD with 41 having choriocarcinoma, 18 molar pregnancies and no case of invasive mole or PSTT. Out of the 41 case folders retrieved, 23 were choriocarcinoma and 18 of molar pregnancies. The prevalence of GTD was 7.2 per 1000 deliveries (0.72% or 1 in 138 deliveries) and constituted 2.4% of gynaecological admissions. Hydatidiform mole (HM) occurred in 1 in 452 deliveries and choriocarcinoma occurred in 1 in 198 deliveries. Ages ranged from 19-49 years with mean of 32.5+ 5.0 years. Most (66.7%) cases of HM were 19-29years while 60.9% of choriocarcinoma cases were 30-39years. Majority of cases were multiparous. The antecedent events predating choriocarcinoma were Hydatidiform mole (31.7%), abortions (29.3%) and 2.4% followed term pregnancy. History of amenorrhea was present in all cases while vaginal bleeding occurred in 97.6%, pallor (87.8%), hyperemesis gravidarum (48.8%) and 4.9% came in shock. Consequently, common complications reported were haemorrhage (90.2%), anemia (87.8%) and shock (12.2%). Pregnancy test was positive in 90.2% of cases and serum beta hCG was done in 24.4% with more than half having a level >12,000miu/ml. All patients had pelvic ultrasound scan and snowstorm appearance occurred in 41% of benign GTD cases. Histology was used to confirm 56.1% cases of choriocarcinoma and 43.9% of molar gestation. Most (94.4%) of HM had suction evacuation while 95.6% of choriocarcinoma cases had chemotherapy, one case (2.4%) had Total Abdominal Hysterectomy. Contraception was used in 78% and common methods were male condom (41.5%) and 36.6% used combined oral contraceptive pills. Less than half (43.9%) had follow up for 6 months and 9.8% were seen for more than a year. Eight patients had subsequent pregnancies and there was one death in the series giving a case fatality of 2.4%. Gestational trophoblastic disease is a significant source of maternal morbidity with increased risk of mortality from complications if not detected early and treated promptly.

Key words: Choriocarcinoma; gestational trophoblastic disease; human chorionic gonadotrophin; hydatidiform mole; placental site trophoblastic disease.

Address for correspondence: Dr. Abimbola Omolara Kolawole, Department of Obstetrics and Gynaecology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.
E-mail: kolabimbo@yahoo.com

Access this article online	
Website: www.tjogonline.com	Quick Response Code
DOI: 10.4103/0189-5117.192228	

How to cite this article: Kolawole AO, Nwajagu JK, Oguntayo AO, Zayyan MS, Adewuyi S. Gestational trophoblastic disease in Abuth Zaria, Nigeria: A 5-year review. Trop J Obstet Gynaecol 2016;33:209-15.

Introduction

Gestational trophoblastic disease (GTD) includes a spectrum of diseases (tumour or tumour-like conditions) characterised by aberrant growth and development of the trophoblasts of placenta that may continue even after the end of pregnancy. GTD encompasses the benign trophoblastic disease (complete and partial moles) and the malignant trophoblastic diseases, including the invasive mole (chorioadenoma destruens), choriocarcinoma and placental-site trophoblastic tumour (PSTT). They are composed of both syncytiotrophoblastic and cytotrophoblastic cells, with the exception of PSTT, which is derived from intermediate trophoblastic cells. In addition to being the first and only disseminated solid tumours that has proved to be highly curable by chemotherapy, they also produce a unique and characteristic tumour marker, human chorionic gonodotropin (HCG).[1-7]

Complete mole, which is genetically 46XX, results from the fertilization of an empty ovum by a haploid sperm followed by duplication or Dispermy 46XY (fertilization of an empty ovum by 2 different sperms). On the other hand, partial mole is usually due to triploidy (69XXY, 69XXX, 69XYY).[8-11] The hydatidiform mole (HM) is characterized pathologically by a bunch of grape-like structures (complete mole has hydropic villi, trophoblastic hyperplasia and absent embryo whereas the partial mole has hydropic villi and fetal parts). The invasive mole is locally invasive and is usually diagnosed due to persistent HCG following approximately 5–10% of all molar pregnancies. Pathologically, molar changes are seen penetrating the myometrium on hysterectomy specimen or ultrasound scan. It is a cause of acute abdomen, haemorrhage and uterine perforation.[9-14]

PSTT arises from the placental bed mostly from intermediate trophoblast, usually following a term pregnancy (1–3 years). It may be benign or malignant, secretes low amount of HCG but high human placental lactogen (HPL) and as such it is not chemosensitive. It rarely metastasizes beyond the uterus.[12-14]

Fifty percent of choriocarcinomas follows HM, whereas abortion and term pregnancy contributes 25% each. It secretes large amount of HCG 100000–400000 units daily causing theca lutein cysts. It is pathologically characterized by haemorrhagic, necrotic tumour, invasive chorion with proliferation of syncytiotrophoblast and cytotrophoblast. It is metastatic but curable with chemotherapy. It is a source of significant morbidity with increased risk of mortality from complication, if not detected early and promptly treated.[12]

Studies have shown that GTD is source of significant morbidity with increased risk of mortality from complications, if not detected early and promptly treated. The incidence of GTDs, especially molar pregnancy, varies by geographic region. For instance, it is generally accepted that, in developing countries, the frequency is much higher.[1,2]

The incidence is higher in women younger than 20 years (teenagers) and older than 40 years of age (40–50 years).[1,3-5] It is also higher in nulliparous women, in patients of low economic status and in women whose diets are deficient in protein, folic acid and carotene.[1] In the far east, figures of 1 in 500 individuals (Singapore), 1 in 294 (Japan) and 1 in 314 (Iran) have been reported. In Ibadan, Nigeria, a high figure of 1 in 205 pregnancies has also been reported.[3]

Molar pregnancy usually presents in the 4th and 5th month of pregnancy and should be suspected in any woman with vaginal bleeding in the first half of pregnancy. This occurs in up to 92% of cases,[1] with passage of vesicles in 60%,[13] abdominal pain, hyperemesis gravidarum, hyperthyroidism or onset of pre-eclampsia prior to 24 weeks of gestation. The absence of fetal heart tones, a uterus too large for the estimated gestational age and presence of theca lutein cysts on physical examination further support the diagnosis.[1,2,12] Honeycomb appearance on ultrasound scan was observed in 84% of the cases in Jos.[13] A high or rising serial beta-HCG determination and histological examination are necessary to establish a firm diagnosis of GTD.[12]

According to the study by Rafindadi *et al*.[8] on the pathomorphology of molar gestation in Zaria (1995–2004), analysis of 56 cases showed complete HM in 34, partial HM in 20 and invasive mole in 2. The frequency of HM was 1 in 612 deliveries. The mean age of the patients was 25.7 years, and their leading mode of presentation was vaginal bleeding during 11–18 weeks of gestation.

The treatment of different GTDs depends on the histological type. Suction evacuation is the most common form of management for HM.[9] Other modes of treatment include chemotherapy, hysterectomy and radiotherapy or a combination of these.[3,4]

Follow up is essential in all cases of GTD and is based on serial levels of HCG hormones, and studies have shown that many of the patients do not return for follow up.[4,5] The disease is of great interest because of its excellent prognosis, if diagnosed and treated on time, as well as the fact that the potential for child bearing can be preserved.[8] Approximately 20% of patients with complete HM would develop malignant sequelae.[5,12] This is lower (12–15%) in studies carried out in Jos, Nnewi and Ile-Ife, which is attributed to poor follow-up, which is as poor as 32%.[13] Contraception is advised to avoid pregnancy during follow up.

Mbamara *et al*. reported low contraceptive compliance among women being followed-up for HM in Nnewi.[9]

Study justification

GTD is a significant source of maternal morbidity with increased risk of mortality from complications if not detected early and treated promptly.[1,2,7] It is hoped that the findings of this study will guide management of such cases in the future. It is also believed that the findings of this study will be used to recommend appropriate strategies to reduce the maternal morbidity and mortality arising from it.

Aim

This study was conducted to document the prevalence, risk factors, clinical presentations, diagnosis, treatment options and outcomes of GTD in Ahmadu Bello University Teaching Hospital (ABUTH).

Objectives

- To determine the prevalence and risk factors of GTD
- To determine the clinical manifestation of GTD
- To assess the management of GTD in ABUTH.

Materials and Methods

A 5-year retrospective study of patients with GTD managed at the ABUTH, Zaria, north-west Nigeria from 1st January, 2008 to 31st December, 2012 was undertaken. The names and hospital numbers of all cases of GTD in the hospital over the 5-year period were obtained from the gynaecology ward and operating theatre registers. The gynaecology ward and labour ward registers also provided information on the total number of gynaecological admissions and deliveries, respectively.

The variables considered included the maternal age at presentation, parity, marital status, as well as gestational age at presentation, risk factors, clinical presentations, investigation/laboratory results, mode of treatment, post-treatment contraception, follow-up and the complications of GTD. These were extracted from the case file obtained from the records department. The data obtained were expressed as percentages, means and standard deviations. The data processing and analysis were carried out using the Statistical Package for the Social Sciences software version 16 (SPSS Inc. Released 2007, SPSS for Windows, Version 16.0. Chicago, SPSS Inc).

Inclusion criteria

All retrievable case files of cases of molar pregnancy managed within the study period.

Exclusion criteria

Those with incomplete records and irretrievable case files were excluded from the study.

Results were discussed and compared with the previous studies conducted elsewhere. Relevant conclusions were drawn from the results.

Results

During the study period, from 1st January, 2008 to 31st December, 2012, there were a total of 59 (18 molar and 41 choriocarcinoma) cases of GTDs that were diagnosed and treated in ABUTH, Zaria. However, only 41 [18 (43.9%) molar and 23 (56.1%) choriocarcinoma] case files were retrieved from the Medical Records Department of the hospital, showing a retrieval rate of 69.5%. There was no case of invasive mole or placental trophoblastic tumour during the period under review. The total number of deliveries in this hospital during the same period was 8138, giving the incidence of GTDs as 0.72% or 1 in 138 deliveries or 7.2 per 1000 deliveries (HM in 1 of 452 whereas choriocarcinoma in 1 of 198 deliveries). Similarly, in the 5-year period of study, there were 2453 gynaecological admissions, and hence, GTD constituted 2.4% of all gynecological admissions.

Table 1 shows the age distribution of the patients. Their ages ranged between 19 and 49 years, with the mean age being 31.5 ± 5 years. The majority of the patients with HM (66.7%) were aged between 19 and 29 years whereas most of those with choriocarcinoma (60.9%) were aged between 30 and 39 years. The parity distribution of the patients ranged between 0 and 10; this is shown in Table 2. The number of multiparous patients were the highest, 21 (51%) patients, followed by grandmultiparous 19 (46%) patients. There were 2 (4.9%) of para ≥10 and only 1 nullipara patient (2.4%). Table 3 shows that most respondents were Hausas (53.7%), Muslims (65.9%), and housewives (58.5%). Most cases of choriocarcinoma (16) 69.5% occurred in grandmultiparous women, whereas only 16.7% (3) of hydatidiform occurred in them. Most of the cases of choriocarcinoma had antecedent events with previous HM being 31.7%, followed by abortion in 29.3%, and only 2.4% followed term pregnancy. All the patients presented with amenorrhoea. However, in addition to amenorrhoea, the most common presenting symptom was abnormal vaginal bleeding, 40 (97.6%), followed by pallor 36 (87.8%), large for gestational age, 31 (75.6%), dizziness 26 (63.4%) and hyperemesis gravidarum 20 (48.8%). Only 2 patients (4.9%) presented with shock. This is shown in Table 4.

Table 1: Age distribution of patients with gestational trophoblastic disease (GTD) seen in Abuth, Zaria over a 5-year period

Age (years)	Benign GTD, *n* (%)	Malignant GTD, *n* (%)
19-29	12 (66.7%)	6 (26.1%)
30-39	5 (27.8%)	14 (60.9%)
40-49	1 (5.5%)	3 (13.0%)
Total	18 (100%)	23 (100%)

Table 2: Parity distribution of patients with gestational trophoblastic disease (GTD) seen in Abuth, Zaria over a 5-year period

Parity	Molar gestation	Choriocarcinoma	Total
0	1	0	1
	2.4%	0.0%	2.4%
1	5	1	6
	12.2%	2.4%	14.6%
2	2	0	2
	4.8%	0.0%	4.9%
3	6	3	9
	14.6%	7.3%	22.0%
4	1	3	4
	2.4%	7.3%	9.8%
5	1	5	6
	2.4%	12.2%	14.6%
6	1	6	7
	2.4%	14.6%	17.1%
7	1	3	4
	2.4%	7.3%	9.8%
>10	0	2	2
TOTAL	18	23	41
	31.7%	56.1%	100%

Table 5 shows the complications observed in patients with GTD. Haemorrhage was the most common 37 (90.2%) followed by anaemia in 36 (87.8%). The other complications included shock in 5 (12.2%) and hypertension 2 (4.9%). Laboratory results showed that 37 (90.2%) of all patients tested positive on pregnancy test. Only 10 (24.4%) had serum beta-HCG and 50% had levels ≥12000 mIU/ml. In this study, all the patients underwent pelvic ultrasound scan. The typical snow storm appearance was described in 17 (41%) of the total cases. Histology confirmed 23 (56.1%) cases of choriocarcinoma and 18 (43.9%) of molar gestation, of which 13 (31.7%) were complete moles; this is depicted in Table 6.

Regarding the treatment options given to patients with GTD, shown in Table 7, almost all the patients with HM [17 out of 18 (94.4%)] had suction evacuation. Approximately 22 out of 23 (95.6%) patients with choriocarcinoma had chemotherapy, whereas only one of the total cases (2.4%) had hysterectomy. Majority of those who were followed up 32 (78.0%) used contraception following treatment. Barrier method using male condom was the most common contraceptive method used in 17 (41.5%) cases followed by combined oral contraceptives in 15 (36.6%).

Table 3: Sociodemographic characteristics of respondents

Characteristics	Frequency	Percentage
Ethnicity		
Hausa	22	53.7
Igbo	2	4.0
Yoruba	5	12.2
Others	12	30.1
Religion		
Christianity	14	34.1
Islam	27	65.9
Marital status		
Married	40	97.6
Single	1	2.4
Educational level		
None	3	7.3
Primary	20	48.8
Secondary	16	39.0
Tertiary	2	4.9
Occupation		
Not indicated	1	2.4
Trader	5	12.2
Civil servant	4	9.8
House wife	24	58.5
Student	3	7.3
Tailor	1	2.4
Teacher	3	7.3

Table 4: Clinical manifestation of patients with gestational trophoblastic disease (GTD) seen in Abuth, Zaria over a 5-year period

Presenting complaints	Frequency	Percentage
Amenorrhoea	41	100
Abnormal vaginal bleeding	40	97.6
Pallor	36	87.8
Large Gestational Age	31	75.6
Hyperemesis gravidarum	20	48.8
Dizziness	26	63.4
Ovarian Enlargement	2	4.9
Urethral Nodule	2	4.9

Table 5: Clinical complication of patients with gestational trophoblastic disease (GTD) seen in Abuth, Zaria over a 5-year period

Complications	Frequency	Percentage
Anaemia	5	12.2
Hypertension	2	4.9
Haemorrhage	37	90.2
Shock	12.2	12.2
Pre-eclampsia/eclampsia	Nil	Nil
Hyperthyroidism/ Thyrotoxicosis	Nil	Nil

The follow-up of patients following treatment is shown in Table 8. Only 18 (43.9%) of the patients had complete post-treatment follow-up for 6 to 12 months, and only 4 cases (9.8%) were followed up for over 1 year, whereas 2 (4.9%) cases were lost to follow-up. Eight of the patients had subsequent pregnancies. There was one maternal death during the period under review, giving a case fatality rate of 2.4%.

Discussion

The prevalence of 7.2 per 1000 deliveries in this study shows that GTD is quite common in our environment. This is higher than 4.7/1000 deliveries reported in Nnewi[10] and 4.06 in Onitsha[15] both in south-east Nigeria. This increased high prevalence of GTD in our centre may be due to the status of a teaching hospital as well as a referral centre from various clinics both private and public. The HM prevalence rate of 1 in 452 deliveries found in this study is similar to 1 in 500 in Singapore but lower than 1 in 357 from Jos, Nigeria.[3,13] This study noted higher incidence of choriocarcinoma than HM. This is similar to the finding in Nnewi, but differs from other studies with higher incidence of HM.[10,13] This may be attributable to the fact that many patients with HM end up at peripheral centres where suction evacuation was enough treatment for them, leaving those with persistent symptoms (mostly choriocarcinoma) to present to our centre, thereby tilting the ratio of patients with GTD in favour of choriocarcinoma.

Maternal age has been reported to influence the risk of GTD with the prevalence being increased in women lower than 20 years and above 40 years of age.[1,3,5] The findings of the study do not support this because women between 30 and 38 years of age formed the majority of the patients. This, however, conforms with the experience of other researchers.[2,11,13] In addition, most of the patients were multiparous, 21 (51%) as found in some studies, but at variance with those of other researcehrs.[4,5,13] This lends credence to the suggestion that parity *per se* may not be an independent factor for the epidemiology of GTD.[10] As expected, choriocarcinoma follows an antecedent event. In this study, most of the cases of choriocarcinoma occurred following previous HM in 31.7%, abortion 29.3% and only 2.4% followed term pregnancy.[21,22,24]

All the patients in this review presented with amenorrhoea similar to the results of previous studies in the literature.[1,10,13-23] This reflects the fact that there is a need for early booking for every patient who ever suspects or confirms that she is pregnant. In addition, there should be an evaluation of all patients with history of amenorrhoea, because with routine first trimester ultrasonography, a significant proportion of patients can be identified,[14,15] although they may be asymptomatic at the time of diagnosis.[2]

Table 6: Histological variants of patients with gestational trophoblastic disease (GTD) seen in Abuth, Zaria over a 5-year period

Histology	Frequency	Percent
Molar gestation complete	13	31.7
Molar gestation partial	5	12.2
Choriocarcinoma	23	56.1
Total	41	100.0

Table 7: Mode of treatment of patients with gestational trophoblastic disease (GTD) seen in Abuth, Zaria

Treatment	Benign GTD	Malignant GTD	Total
Suction evacuation only	17	0	17
	41.5%	0.0%	41.5%
Hysterectomy only	0	1	1
	0.0%	2.4%	2.4%
Chemotherapy	1	22	23
	2.4%	53.7%	56.1%
Total	18	23	41
	43.9%	56.1%	100.0%

Table 8: Follow-up of patients with molar pregnancy seen in Abuth, Zaria

Duration	Frequency	Percentage
Not indicated	1	2.4
0-1 month	2	4.9
1-6 months	14	34.1
6-12 months	18	43.9
>12 months	4	9.8
Lost to follow up	2	4.9
Total	41	100.0

In addition to amenorrhoea, this study revealed that the most common clinical manifestation of molar pregnancy was abnormal vaginal bleeding. This occurred in more than 97.6% of cases. This agrees fully with documentations in the literature where more than 90% of patients with molar pregnancies present with abnormal uterine bleeding, usually during the first trimester.[2,3,12,20,23]

In addition, a "large for gestational age" uterus was observed in more than 70% of the cases with GTD seen in our centre. This finding was corroborated by the observation in the literature where approximately half of the patients with molar pregnancy have uterine size that are greater than the appropriate size for their gestational age.[3,20,23]

Regarding the complications associated with molar pregnancies, this study has demonstrated that haemorrhage

(90.2%) was the most common complication, followed by anaemia and shock. These findings are similar to the study in Onitsha where haemorrhage was the most common complication.[15] Anaemia could result from late presentation following abnormal uterine bleeding or late booking of so-called ongoing pregnancy. It could also result from severe haemorrhage occurring during the evacuation process or as a result of post-evacuation chemotherapy.[2,3] The shock observed in these patients could also be as a result of the haemorrhage.

This study has also demonstrated that all the cases of GTD reviewed were diagnosed by pelvic ultrasound scan. Therefore, the importance of ultrasound in the management of patient with suspected GTD cannot be over-emphasised. As reported earlier, an ultrasound scan should be obtained in any patient who presents with vaginal bleeding in the first half of pregnancy and has a uterus greater than 12 weeks gestational size.[3] However, even when the uterus is appropriate for gestational age, ultrasound scan can be the key in differentiating factor between a normal pregnancy and a GTD.[3]

Another important investigation which is both essential in the diagnosis and management of GTD is serum beta-HCG determination by radioimmunoassay. It measures the beta-HCG which is more sensitive and specific than urinary beta-HCG.[1,3] However, this was done in only 24.4% of the cases (who could afford a private laboratory due to lack of facilities for radioimmunoassay where many of these cases were managed). More than 50% of them had levels greater than 12000 mIU/ml. The rest of the patients had urinary beta-HCG determined by pregnancy test in "neat and dilution" and 90.2% had a positive test.

In this study, suction evacuation was employed in the management of HM in our centre and was done in more than 94% of cases. This finding was in agreement to the Royal College of Obstetrician and Gynaecologists' practical guidelines on the management of complete molar pregnancy.[1,2,12,27] Suction evacuation is safe, rapid and effective in nearly all cases of HM.[2,3,20-26] In our centre, 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. It is also done for older women with HM who are more likely to develop malignant sequelae.[3,13] This patient had hysterectomy because she had an uncontrollable haemorrhage at presentation.

It was noted that the majority of the patients (78.0%) received post-treatment contraception and barrier contraception, with male condoms as the most common contraceptive method used by the study patients. These findings differ from those presented in other studies.[9,10,13] After completion of the treatment, the use of contraceptive is recommended so that pregnancy is avoided for 12 months to minimize the confusion over disease relapse from HCG produced in pregnancy.[1,2,6]

In this review, only 43.9% of the patients had complete post-treatment follow-up for at least 6 months and only 9.8% cases were followed-up for more than 1 year. It is recommended that patients should be seen initially weekly, monthly and then every 3 months intervals for a total of one year.[2,3,6] A follow-up period longer than one year is not necessary for benign GTD.[2,16-19,27] During each visit, a clinical examination should be carried out. The serum B-subunit HCG assay is performed,[8,17-19] and a chest X-ray is repeated if indicated.[2,3]

The case fatality rate in our study was 2.4%. This is high when compared with other studies where there were no recorded maternal deaths.[12,14] In this study, the maternal death occurred in patients who had very severe shock and had irreversible shock at presentation and after evacuation.

Conclusion

There was a high prevalence of GTD in our tertiary health institution during the period of study. It is an important cause of maternal morbidity and mortality in our centre. There is need for early recognition, timely referral and prompt and proper management of this condition. Adequate follow-up of the patients is mandatory.

One of the limitations of this study was that the incidence of subsequent pregnancies after complete treatment of molar pregnancies was not studied. Moreover, it was a retrospective study with attendant set-back of incomplete information. Finally, there was poor follow-up and a lot of case files could not be retrieved.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Aghajanian P. Gestational Trophoblastic Disease. In: Decherney AH, Nathan L, Godwin TM, Laufer N, editors. Current Diagnosis Treatment in Obstetrics and Gynaecology. 10th Ed. New York: Mc Craw Hill Medical Publishing Division; 2007. p. 885-95.
2. Savage P, Seckl M. Trophoblastic Disease. In: Edmund KD, editor.

Dewhurt's Textbook of Obstetrics and Gynaecology. 7th Ed. UK: Black Well publishing, Inc.; 2007. p. 117-24.
3. Agboola A. Trophoblastic Tumours. Textbook of Obstetrics and Gynaecology for medical students. 2nd Ed. Ibadan, Nigeria: Heinemann Educational Books; 2006. p. 218-24.
4. Savage P. Molar pregnancy. The Obstetrist and Gynaecologist 2008;10:3-8
5. Sebire NJ, Foskett M, Fisher RA, Rees H, Seckl M, Newlands E. Risks of partial and complete hydatidiform molar pregnancy in relation to maternal age. BJOG 2002;109:99-102.
6. Sebire NJ, Foskett M, Fisher RA, Rees H, Seckl M, Newlands E. Risks of recurrent hydatidiform mole and subsequent pregnancy outcome following complete or partial hydatidiform molar pregnancy BJOG 2003;110:22-6.
7. de Andrade JM. Hydatidiform mole and gestational trophoblastic disease. Rev bras Ginecol Obstet 2009;31:94-101.
8. Hou JL, Wan XR, Xiang Y, Qi QW, Yang XY. Changes of clinical features in hydatidiform mole: Analysis of 113 cases. J Reprod Med 2008;53:629-33.
9. Mayun AA, Rafindadi AH, Shehu MS. Pathomorphology of molar gestation in Zaria. Niger Med J 2010;51:1-4.
10. Mbamara SU, Obiechina NJ, Eleje GU, Akabuike CJ, Umeononihu OS. Gestational trophoblastic disease in a Tertiary Hospital in Nnewi, Southeast, Nigeria. Niger Med J 2009;50:87-9.
11. Chakrabarti BK, Mondel NR, Chatterjee T. Gestational trophoblastic tumour at a tertiary level cancer center: A retrospective study. J Reprod Med 2006;51:875-8.
12. Page RD, Kudella AP, Freedman RS, Kavanagh RJ. Gesational trophoblastic tumours. Medical Oncology: a comparative review. 8th ed. Oncology 2005.
13. Ocheke AN, Musa J, Uamai AO. Hydatidiform mole in Jos, Nigeria. Niger Med J 2011; 52:223-6.
14. Bugti QA, Baloch N, Baloc MA. Gestational trophoblastic disease in Quetta. Pak Med Res 2005;44:200.
15. Obiechina NJ, Udigwe GO, Obi RA. Molar pregnancy a ten year review at Onitsha Nigeria. Journal of Medical Investigation and Practice JOMIP 2001;13:26-31.
16. Thirmagal B, Sinha D, Bhatti N. GTN: Are we compliant with the standard. Obstet Gynaecol 2009;29:434-6.
17. Gerulath AH. Gestational trophoblastic disease. Society of Obstetricians and Gynaecologist of Canada (SOGC) Clinical Practice Guidelines No 114; May 2002.
18. Semer DA, Macfee MS. Gestational trophoblastic disease: Epidemiology. Semin Oncol 1995;22:109-13.
19. Mourali M, Fkih C, Essoussi-Chikhaoui J, Ben Haj Hassine A, Binous N, Ben Zineb N, *et al*. Gestational tropholastic disease in Tunisia. Tunis Med 2008;86:665-9.
20. Osamor JO, Oluwasola AO, Adewole IF. The clinicopathological study of complete and partial hydatidiform moles in a Nigerian population. Obstet Gynaecol 2002;22:423-5.
21. Eniola OA, Mabayoje P, Ogunniyi SO. Hydatiform mole in Ile-Ife, Nigeria: A 10 year review. J Obstet Gynaecol 2001;21:405-7.
22. Egwuatu VE, Ozumba BC. Observations on molar pregnancy in Enugu, Nigeria. Int J Gynaecol Obstet 1989;29:219-25.
23. Aboyeji AP, Ijaiye MA. Hydatidiform mole in Ilorin, Nigeria: A ten year review. Nig J Med 2000;19:56-60.
24. Attah EB. Hydatidiform mole. In: Human Pathology. 1st Ed. Ibadan: Ibadan University Press; 2000. p. 519-22.
25. Mayun AA. Gestational trophoblastic disease in Zaria. A ten year histopathological review. FMC Pathology dissertation. National Postgraduate Medical College of Nigeria; May 2003.
26. Kim MJ, Kim KR, Ro JY, Lage JM, Lee HI. Diagnostic and pathogenetic significance of increased stromal apoptosis and in complete vasculogenesis in complete hydatidiform moles in very early pregnancy periods. Am J Surg Pathol 2006;30:362-9.
27. Royal college of Obstetricians and Gynaecologists. The Management of Gestational Trophoblastic Neoplasia. Green Top Guideline No. 38. London: RCOG; 2004.