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Morphological Pattern of Gestational Trophoblastic Disease in the University of Benin Teaching Hospital, Benin City: A Twenty Year Review (1993 – 2012)

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Authors' contributions

This work was carried out in collaboration between both authors. Author IO designed the study, wrote the protocol and wrote the first draft of the manuscript. Author EEU managed the literature searches and SPSS data analyses of the study. The histopathologic slides were jointly reviewed by both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Gestational trophoblastic disease (GTD) is a spectrum of proliferative disorders of the placental trophoblast with a range of histological appearance and clinical behaviour. Although its aetiopathogenesis is as yet incompletely understood, it is well established that early detection and prompt treatment lead to the preservation of normal health and fertility.
Aim and Objectives: This study sought to determine the morphological pattern as well as the age and site distribution of the various forms of GTD histologically diagnosed in the University of Benin Teaching Hospital, Benin City, between January 1993 and December 2012. It is a hospital based, retrospective review utilizing materials from the archives of the Department of Morbid Anatomy, University of Benin Teaching Hospital.
Results: A total of 168 cases of GTD were encountered, and 103 (61.3%) of these were seen in the latter 10 years, reflecting a rise in incidence in recent years. The age range was 15 – 62 years,

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and the mean age was 31.27 ± 7.36 years. GTD was found to be less common at the extremes of reproductive age, with the peak prevalence being in the third and fourth decades. Partial mole was commonest (52.4%), followed by complete mole (25.0%) and choriocarcinoma (19.0%). The ratio of the benign to malignant lesions was 4:1. The uterus was the commonest site of GTD accounting for 83.3% of cases, while 16.6% of cases were distributed among ectopic sites. There was failure to clinically or grossly identify molar vesicles in 80.6% of cases of hydatidiform mole; this highlights the relevance of histopathological examination of products of conception of both intrauterine and ectopic gestation.

Conclusion: The prevalence of GTD appears to have been rising in this environment in the recent years.

Keywords: Gestational trophoblastic disease; morphological pattern; Benin City.

1. INTRODUCTION

Gestational trophoblastic disease (GTD) refers to a spectrum of proliferative disorders of the placental trophoblast, with a wide range of histological appearance and clinical behaviour [1]. The World Health Organization (WHO) classification of gestational trophoblastic diseases [2,3] includes hydatidiform mole (partial, complete, and invasive), tumours (gestational choriocarcinoma, placental site trophoblastic tumour and epithelioid trophoblastic tumour) and tumour-like conditions, including exaggerated placental site, placental site nodule or plaque [4,5,6].

The aetiology and pathogenesis are not well understood; however, GTD has been associated with ethnicity, extremes of reproductive age, prior molar pregnancy, lower socioeconomic class, and diet. Studying GTD should be of great interest because of its excellent prognosis if diagnosed early and treated promptly, especially as there is great potential for the preservation of both a healthy life and normal fertility [7].

GTD is reported to have the highest incidence in Africa and Asia and the lowest incidence in Western Europe and North America, [8] and so it appears to be a problem of the less developed areas of the world. Results of studies done in Nigeria show that GTD is fairly common among Nigerian women of reproductive age, and the following figures quickly reveal the magnitude of the problem and provide statistical evidence as to why GTD should be so studied: 1 in 172 deliveries in Ibadan, 1 in 184 in Lagos, 1 in 357 in Jos, [9] 1 in 166 in Gombe [10] and 1 in 252 from a study carried out a few decades ago in Benin [11]. Moreover, many of the studies were mostly on hydatidiform mole [9,10] rather than on the entire spectrum of GTD, raising the possibility that although other forms of GTD may be less common, these reported incidences could have been even higher had choriocarcinoma and the less common forms of GTD been included in the calculations.

2. MATERIALS AND METHODS

The study was done in the Department of Morbid Anatomy, UBTH. This hospital is the major tertiary care hospital and referral centre in the Benin metropolis, having well established obstetric, gynaecological and histopathology departments, and serving as catchment centre to neighbouring states.

Data regarding specimens diagnosed as GTD following endometrial curettage for incomplete abortion, as well as records of any invasive, extrauterine or metastatic GTD diagnosed in the Morbid Anatomy Department of the University of Benin Teaching Hospital (UBTH), between January 1993 and December 2012, were the materials for this study.

These were specimens received from the Department of Obstetrics and Gynaecology, UBTH, other hospitals within the Benin City metropolis and within Edo State, as well as from neighbouring states.

Data including age, nature of specimen, and preoperative diagnosis were retrieved from the departmental surgical day books for the years under review. Slides were retrieved from the archives and the paraffin blocks corresponding to the recorded histology numbers were retrieved and fresh slides were prepared when necessary.

Diagnosis and classification were according to the World Health Organization (WHO) recommendations.

The data was analyzed using the statistical package for social sciences (SPSS, V.16.0,

Incorporated, Chicago, Illinois, USA), with representative tables. Cases of missing records, slides and paraffin blocks were excluded from the study.

3. RESULTS

During the period of study a total of 33,454 surgical specimens were received and diagnosed in the Department of Histopathology, University of Benin Teaching Hospital. Of these, 168 (0.5%) cases diagnosed as entities under gestational trophoblastic disease (GTD) were included in the study.

The age of the patients was 15 – 62 years, with a mean age of 31.27 ± 7.36 years, a median age of 30 years and a modal age of 28 years. As shown in Table 1, the peak age of GTD was found to be the 20–29 year age group, with 76 cases accounting for 45.2%, closely followed by the 30–39 year age group with 64 cases (38.1%). The three major diagnostic entities of GTD in this study, namely partial mole, complete mole and choriocarcinoma, all had their peak ages at 20 – 29 years, closely followed by 30 – 39 years.

The uterus was the major site for GTD as evidenced by 137 cases (81.5%), followed by the fallopian tubes with 25 cases (14.9%). The right fallopian tube was more commonly affected than the left, with 17 (10.1%) and 8 (4.8%) cases respectively. Occasional cases were found elsewhere in the ovaries (3), cervix (2), and vagina (1). These findings are displayed in Table 3. Of note was the fact that of the 134 cases of hydatidiform mole diagnosed, molar vesicles were detected by ultrasonography or clinical observation of the endometrial tissue or products of conception in only 26 cases (19.4%).

Most cases of GTD were of the benign variety; as outlined in Table 4, the ratio of benign to malignant GTD was 4:1. All the cases of benign GTD were hydatidiform moles, with partial, complete and invasive mole together making up 134 cases (79.8% of GTD). Partial mole was the commonest form of benign GTD encountered, accounting for 88 cases (52.4%), followed by complete mole (42 cases; 25.0%) and 4 cases of invasive mole (2.4%). The remaining 34 cases (20.2%) were malignant, with choriocarcinoma accounting for most of the cases (n=32, 19%) and one case each of placental site trophoblastic tumour and epithelioid trophoblastic tumour.

4. DISCUSSION

The overall incidence of gestational trophoblastic disease has been reported to be higher in developing areas of the world [8,12] such as our study area, where the increased utilization of histopathology services in recent years might have created an impression of the incidence rising even higher. Rather than the hospital based studies commonly undertaken in Nigeria, there is the need for population based studies on GTD with a view to determining a more accurate incidence and prevalence in our environment.

This review included 168 cases of GTD over a twenty-year period, with 103 (61.3%) of the cases occurring in the latter ten years. An earlier ten-year study here in Benin [11] had revealed 48 cases of GTD. It becomes obvious therefore from the foregoing that its incidence appears to have been on the increase in recent years. This finding may be attributable to increasing awareness and utilization of histopathology services in this region rather than an actual rise in the incidence of GTD.

It is well known that gestational trophoblastic lesions are nearly always disorders of the reproductive years [13,14,15]. Women who are sexually active are at risk of developing GTD [15]. Most of the cases of GTD are clustered in the reproductive age group as evidenced by the age distribution in this study. Only 3 out of the 168 cases occurred after the age of 49.

Table 1. Age group distribution of forms of GTD

Diagnosis	Age group						
	0-19	20-29	30-39	40-49	50-59	60-69	Total
Partial mole	2	39	38	7	1	1	88
Complete mole	2	17	15	8	0	0	42
Invasive mole	0	4	0	0	0	0	4
Choriocarcinoma	0	15	11	5	1	0	32
Placental site trophoblastic tumour	0	1	0	0	0	0	1
Epithelioid trophoblastic tumour	1	0	0	0	0	0	1
Total	**5**	**76**	**64**	**20**	**2**	**1**	**168**

Table 2. Frequency distribution of the various types of specimens received

	Frequency	Percent (%)
Products of conception	89	53.0
Uterus	19	11.3
Left fallopian tube	8	4.8
Right fallopian tube	16	9.5
Endometrial tissue	29	17.3
Unspecified	6	3.6
Left ovary	1	0.6
Total	168	100.0

The mean age for GTD in this study was 31.27 years, similar to a mean of 31 years reported by Mbamara et al. [7] but higher than 28.5 and 27.97 years reported by Moodley et al. [16] and Al Alaf et al. [15] respectively. The mean ages for partial and complete mole were similar, being 31.08 and 31.62 years respectively. These figures are similar to 31.8 years reported as the mean age for hydatidiform mole in Ile-ife, [8] somewhat higher than 28 years reported in Ibadan [17] and Jos, [9] but much higher than 25.7 and 25 years reported in Zaria [18] and Morocco [19] respectively. The mean age of 31.62 years observed for complete mole in this study is slightly higher than 29.6 years reported in Uganda [20] and much higher than 26 years reported in Syria [21]. These variations among mean ages might probably be at least partly accounted for by geographical, environmental and racial factors [12]. While the factors and mechanisms that determine the age of onset are not entirely clear, it is probable that the interaction between genetics and environment plays a significant role.

Some studies in various parts of the world have revealed GTD to be commoner at the extremes of reproductive age, for example, studies in Ile-ife, Nigeria, [8] Uganda, [20] Pakistan, [22] and Hawaii [23]. Nevertheless, the results of this study suggest that GTD in all its common forms is commonest at the peak of reproductive life: the peak age for GTD in this study was in the 20 – 29 year age group (45.2%), followed by the 30 – 39 year age group (38.1%). This is corroborated by findings from Iraq [15] and South Africa [16].

Majority of the specimens received in the laboratory were labeled products of conception (53%), endometrial tissue/curettage (17.3%), and uterus (11.3%), and these proportions vary widely with 30%, 8.9% and 3.6% respectively, reported in a study in Zaria [18]. The variation with the study in Zaria is probably due to non-inclusion of choriocarcinoma. That same study on hydatidiform mole reveals that there was failure to clinically or grossly identify molar vesicles in 45% of cases of histologically diagnosed hydatidiform mole; the corresponding

Table 3. Site distribution of GTD

Site	Diagnosis						
	Partial mole	Complete Mole	Invasive mole	Chorio	PSTT	ETT	Frequency (%)
Uterus	67	39	1	28	1	1	137(81.5)
Cervix	0	0	0	2	0	0	2(1.2)
Vagina	0	0	0	1	0	0	1(0.6)
Right fallopian tube	14	2	1	0	0	0	17(10.1)
Left fallopian tube	5	1	1	1	0	0	8(4.8)
Right ovary	1	0	0	0	0	0	1(0.6)
Left ovary	1	0	1	0	0	0	2(1.2)
Total	88	42	4	32	1	1	168(100)

Table 4. Frequency distribution of benign and malignant GTD

	Frequency	Percent (%)
Benign GTD n = 134 (79.8%)		
Partial mole	88	52.4
Complete mole	42	25.0
Invasive mole	4	2.4
Malignant GTD n = 34 (20.2%)		
Choriocarcinoma	32	19.0
Placental site trophoblastic tumour	1	0.6
Epithelioid trophoblastic tumour	1	0.6
Total	**168**	**100.0**

figure in this study was 80.6%, while an earlier study in Benin had reported 64.4% [11]. Despite these variations, it is clear that histopathological examination of products of conception is a necessity, otherwise, many cases of GTD will be missed or have delayed diagnoses.

GTD can arise primarily from any possible site of conception and implantation. Although the uterus is quite understandably the commonest site of occurrence, the total number of cases of ectopic GTD in this work was as high as 28 cases (16.67%). It would however appear from the existing literature that GTD arising from ectopic sites is rather uncommon, [24] much less common than the current study suggests: for example, a study in Gombe [10] revealed no case of ectopic mole, while another in Zaria [18] revealed just one case of an ectopic mole. However, these were retrospective studies carried out in Northern Nigeria over much shorter periods, and dealing with far fewer cases of GTD than in this study (34 cases over 5 years, and 56 cases over 10 years respectively). One study done in Venezuela revealed 18 cases (22.8%) of GTD out of 79 ectopic pregnancy cases studied [25].

In general, the overall management of GTD is interdisciplinary, with the pathologist playing a crucial and sensitive role. In most cases, exact histopathological diagnosis of the trophoblastic lesion remains the gold standard for guiding clinical therapy. Although there are now advanced ancillary diagnostic techniques (mostly in developed areas of the globe) to serve as adjuncts to refine the traditional morphology–based diagnoses, currently, there are no reliable immunohistochemical, genetic or molecular biologic markers for predicting aggressive behavior for hydatidiform mole [26].

With the dearth of advanced ancillary diagnostic techniques in resource-poor areas, it is imperative that pathologists practicing in such centres continue to keep abreast of the morphological diagnostic criteria for the various forms of GTD. In this study, the diagnosis and classification of GTD were done according to the World Health Organization classification. Partial mole was the commonest manifestation of GTD in this review, accounting for 52.4% of all cases. This compares favourably with the findings of a study by Aligbe et al. [11] in which partial mole was the commonest lesion, contributing 47.9% of all cases of GTD. A study in Damascus, Syria, even revealed partial mole to constitute 60% of GTD, the significance of this being that partial mole is less likely to progress to choriocarcinoma than complete mole [21]. On the contrary, Al Alaf et al. [15] reported complete mole to be the commonest form of GTD, accounting for as high as 82.5%, while partial mole made up only 10%. Also, Horn and Bilek [26] reported complete mole as the commonest manifestation of GTD with 69.6%. The diversity among the results may be due to the limitations of routine H & E diagnosis when used alone, and also to lack of strict and uniform diagnostic criteria among the researchers (intra- and inter-observer variation).

The finding of 88 cases of partial mole and 42 cases of complete mole in this study puts the ratio of partial to complete mole at about 2.1:1. Similar ratios of 2.2:1 and 2:1 are reported in Hawaii [23] and Tunis [12] respectively, and less comparable ratios of 2.8:1, 1.5:1 and 1.5:1 are reported in Ireland, [27] Syria [21] and Calabar [28] respectively. Unlike in this and other studies where there are a lot more partial than complete moles, still other studies reveal, to varying degrees, more complete than partial moles. The complete to partial mole ratio is reported as 4.1:1 in Ile-ife, [8] 1.7:1 in Zaria [18] and 10.3:1 in Hong Kong [29]. Two Nigerian studies in Ibadan [17] and Gombe [10] reveal almost equal numbers of complete and partial moles, with ratios close to 1:1.Choriocarcinoma constituted 32 cases (19%) of GTD in this study, and was the third commonest form. A German [26] study also found 32 cases of choriocarcinoma accounting for 20.25% (second commonest form of GTD). Curiously however, a study in Nnewi [7] reported choriocarcinoma to be the most prevalent form of GTD, accounting for as high as 66.7% of cases, and hydatidiform mole 33.3%. Furthermore, a study in Zaria [18] revealed choriocarcinoma to be the commonest form of GTD, making up 43 (37%) of the 99 cases seen. Possible reasons for such may be late presentation at a time when benign GTD had already evolved into malignant neoplasia, although choriocarcinoma is also known to arise sequel to antecedent normal pregnancy, in which case genetic, dietary and geographical, as well as other yet poorly understood risk factors may be more important.

The least common forms of GTD seem to be the rare malignant lesions like the placental site trophoblastic tumour and epithelioid trophoblastic tumour, the benign placental site nodule and exaggerated placental site reaction, and the invasive mole. In this review, 4 cases (2.4%) of

invasive mole were identified, as were 1 case (0.6%) each of placental site trophoblastic tumour and epithelioid trophoblastic tumour. In favourable comparison, studies in Zaria [18] and Malaysia [30] found 2 cases (2.0%) and 1 case (2.6%) of invasive mole respectively; but in contrast, a study in Pakistan [22] found 7 cases (23.3%) out of 30 cases of GTD studied, while another in Germany [26] revealed 13 (8.2%) out of 158 cases of GTD. Studies on hydatidiform mole in Gombe [10] and Miduguri [31] report no cases of invasive mole. Studies on both benign and malignant GTD by Mbamara [7] et al. and Nizam [22] et al. reveal no cases of placental site trophoblastic tumour, but Horn and Bilek report in a German [26] study 1 case (0.6%) of placental site trophoblastic tumour, just as in this work, and 2 cases (1.3%) of placental site nodule (none found in the current study).

Most cases in this review were benign, giving a benign to malignant ratio of almost 4:1. This ratio is similar to 3.8:1 reported in Germany, [26] but is lower in comparison to 2:1 in Zaria, [18] and 2.3:1 in South Africa, [16] and much lower at 1:2 in Nnewi [7] where most of the lesions were malignant. The ratio of benign to malignant GTD is as high as 12:1 and 14:1 in Northern Iraq [15] and Pakistan [22] respectively, where relatively few cases of malignant GTD were reported.

5. CONCLUSION

GTD continues to be an important spectrum of diseases affecting women of mainly the reproductive age, especially in developing countries like Nigeria. Although GTD is reported to have become less of a health problem in recent years in advanced countries, the same certainly cannot be said of developing areas like our environment, where the prevalence appears to have been rising in recent years. Histological examination of products of both intrauterine and ectopic gestation continues to be essential for confirmation of diagnosis. Ancillary investigations, including molecular and genetic studies where available are also very helpful.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval for this study was obtained from the University of Benin Ethics and Research Committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hui P, Martel M, Parkash V. Gestational trophoblastic diseases: recent advances in histopathologic diagnosis and related genetic aspects. Adv Anat Pathol. 2005; 12:116-125.
2. Mazur MT, Kurman RJ. Gestational trophoblastic disease. In: Kurman RJ (ed). Blaustein's pathology of the female genital tract. 4th ed. New York. Springer-Velag. 1994;1049-1093.
3. Silverberg SG, Kurman RJ. Gestational trophoblastic disease. In: Silverberg SG, Kurman RJ (eds). Atlas of tumour pathology. Tumours of the uterine corpus and gestational trophoblastic disease. Armed Forces Institute of Pathology: Washington, DC. 1991;219-287.
4. Shih IM, Kurman RJ. Epithelioid trophoblastic tumour: A neoplasm distinct from choriocarcinoma and placental site trophoblastic tumour simulating carcinoma. Am J SurgPathol. 1998;22:1393-1403.
5. Shih IM, Seidman JD, Kurman RJ. Placental site nodule and characteristics of a distinctive type of intermediate trophoblast. Hum Pathol. 1999;30:687-694.
6. Shih IM, Kurman RJ. The pathology of intermediate trophoblastic tumours and tumour-like conditions. Int J Gynecol Pathol. 2001;20:31-47.
7. Mbamara SU, Obiechina N, Eleje GU, Akabuike CJ, Umeononihu OS. Gestational trophoblastic disease in a tertiary hospital in Nnewi, southeast Nigeria. Niger Med J. 2009;50:87-89.
8. Eniola OA, Mabayoje P, Ogunniyi SO. Hydatidiform mole in Ile-Ife, Nigeria: A 10-year review. J Obstet Gynaecol. 2001; 21:405-407.
9. Ocheke AN, Musa J, Uamai AO. Hydatidiform mole in Jos, Nigeria. Niger Med J. 2011;52:223-226.
10. Mayun AA. Hydatidiform mole in Gombe: a five year histopathological review. Niger J Clin Pract. 2008;11:134-138.
11. Aligbe JU, Ekanem VJ, Akhiwu WO, Banjo AA. Gestational trophoblastic disease (GTD): A ten year review of clinicopathologic features of cases seen at the University of Benin Teaching Hospital, Benin City. Ann Biomed Sci. 2002;1:94-99.

12. Ben Temime R, Chechia A, Hannachi W, Attia L, Makhlouf T, Koubaa A. Clinical analysis and management of gestational trophoblastic diseases: A 90 cases study. Int J Biomed Sci. 2009;5:321-325.
13. Hando T, Ohno M, Kurose T. Recent aspects of gestational trophoblastic disease in Japan. Int J Gynaecol Obstet. 1998;60:71–76.
14. Shih IM, Marzur MT, Kurman RJ. Gestational trophoblastic tumors and related tumor-like lesions. In: Kurman RJ, Ellenson LH, Ronnett BM (eds). Blaustein's pathology of the female genital tract. 6th ed. New York. Springer. 2011; 1076-1126.
15. Al Alaf SK, Omer DI. Prevalence and clinical observations of gestational trophoblastic diseases in a maternity teaching hospital in Erbil City. Trans Biol Biomed. 2010;3:190-199.
16. Moodley M, Tunkyi K, Moodley J. Gestational trophoblastic syndrome: An audit of 112 patients. A South African experience. Int J Gynaecol Cancer. 2003; 13:234-239.
17. Osamor JO, Oluwasola AO, Adewole IF. A clinico-pathological study of complete and partial hydatidiform moles in a Nigerian population. J ObstetGynaecol. 2002;22: 423-425.
18. Mayun AA, Rafindadi AH, Shehu MS. Pathomorphology of molar gestation in Zaria. Niger Med J. 2010;51:1-4.
19. Boufettal H, Coullin P, Mahdaoui S, Noun M, Hermas S, Samouh N. Complete hydatidiform mole in Morocco: Epidemiological and clinical study. J Gynecol Obstet Biol Reprod. 2011;40:419-429.
20. Kaye DK. Gestational trophoblastic disease following complete hydatidiform mole in Mulago Hospital, Kampala, Uganda. Afr Health Sci. 2002;2:47–51.
21. Bashabsheh MA. Maternal age-related rates of gestational trophoblastic disease in a sample from Department of Obstetrics and Gynaecology at Damascus University. Eur J Sci Res. 2011;55:521-526.
22. Nizam K, Haider G, Memon N, Haider A. Gestational trophoblastic disease: Experience at Nawabshah hospital. J Ayub Med Coll Abbottabad. 2009;21:94-97.
23. Jacobs PA, Hunt PA, Matsuura JS, Wilson CC, Szulman AE. Complete and partial hydatidiform mole in Hawaii: Cytogenetics, morphology and epidemiology. BJOG. 2005;89:258-266.
24. Khilifi A, Mkhinini I, Yacoubi M T, Khairi H. A cornual invasive hydatidiform mole: A literature review. Medical Journal Armed Forces India; 2016.
25. Tasha I, Kroi E, Karameta A, Shahinaj R, Manoku N. Prevalence of gestational trophoblastic disease in ectopic pregnancy. Journal of Prenatal Medicine. 2010; 4(2):26.
26. Horn L, Bilek K. Clinicopathologic analysis of gestational trophoblastic disease – report of 158 cases. Gen Diagn Pathol. 1997;143:173-178.
27. Jeffers MD, O'Dwyer P, Curran B, Leader M, Gillan JE. Partial hydatidiform mole: A common but underdiagnosed condition. A 3-year retrospective clinicopathological and DNA flow cytometric analysis. Int J Gynecol Pathol. 1993;12:315-323.
28. Ekpo MD. Hydatidiform mole in Nigeria. J Obstet Gynaecol. 1990;10:363-366.
29. Lai CY, Chan KY, Khoo US, Ngan HY, Xue WC, et al. Analysis of gestational trophoblastic disease by genotyping and chromosome in situ hybridization. Mod Pathol. 2004;17:40-48.
30. Cheah P, Looi L, Sivanesaratnam V. Hydatidiform molar pregnancy in Malaysian women: A histopathological study from the University Hospital, Kuala Lumpur. Malays J Pathol. 1993;15:59-63.
31. Audu BM, Takai IU, Chama CM, Bukar M, Kyari O. Hydatidiform mole as seen in a university teaching hospital: A ten year review. J Obstet Gynaecol. 2009;29:322-325.

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