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Original Research Article

Management of Choriocarcinoma in a Tertiary Institution in North West Nigeria

Constance E Shehu*, Joel C Omembelede, Daniel C Nnadi, Ibrahim G Ango

Department of Obstetrics and Gynaecology, Usmanu Danfodiyo University Teaching Hospital, PMB2370, Sokoto, Sokoto State, Nigeria

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***Corresponding author:** Constance E Shehu

Abstract

The diagnosis of cancer in Nigeria is perceived as a hopeless situation and is not unusual to expect total mortality of all sufferers. Choriocarcinoma is particularly important because it is nearly completely curable. The aim of this study was to review the socio-demographic characteristics, cost implications and management of choriocarcinoma in a tertiary institution in North-west Nigeria. This was a 5-year retrospective study. Records of the patients diagnosed with choriocarcinoma from 1st January, 2008 to 31st December, 2012 were retrieved and relevant data extracted and analyzed using the SPSS for windows version 20.0. There were 24 cases of choriocarcinoma giving an incidence of 1.5 per 1000 deliveries. The mean age of the patients was 33.21 ± 2.14 years. Recurrent vaginal bleeding (95.2%) was the most common form of presentation. The common predisposing factors were complete mole (47.6%) and abortion (28.6%) while the metastatic sites were the vagina/pelvic structures (42.9%) and lungs (33.3%). Many, (33.3%) signed against medical advice (SAMA) while 61.9% had methotrexate or MAC as first-line treatment. The common complications were disease progression despite treatment (33.3%) and myelosuppression (33.3%). The average cost of treatment was ₦200,000 ($600). The 5-year survival rate was 9.5%. The incidence of choriocarcinoma in this review was low. The cost of treatment was out of reach of most patients hence the need for health insurance coverage of all Nigerians. The use of methotrexate and MAC regimen as first-line chemotherapy appeared to be ineffective as the disease progressed despite treatment. The five-year survival was dismal.

Keywords: Choriocarcinoma, incidence, chemotherapy, health insurance, 5-year survival, Sokoto.

INTRODUCTION

Cancer is a worldwide problem and one of the leading causes of death and disability [1]. However, while cancer management has evolved with a high survival rate, it is yet to improve in developing countries. In Nigeria, diagnosis of cancer is perceived as a hopeless situation and is not unusual to expect 100% mortality [2]. Choriocarcinoma is particularly of concern because it is one of the first cancers with improved diagnosis and improved prognosis. It is nearly curable, with 100% cure for cases without metastasis and 65-90% cure for patients with metastatic disease [3].

Choriocarcinoma belongs to the malignant end of the spectrum of chorionic neoplasm that may be gestational or non-gestational [4]. Most choriocarcinoma are associated with pregnancy and may therefore follow any gestational event such as molar pregnancy, abortion, term pregnancy or ectopic pregnancy [5].

It is more common among women of Asian and African descent when compared with their European and North American counterpart, and this may be related to diet and poverty [6]. In Nigeria, the disease is more common in Ibadan, South West Nigeria where it is the second most common genital malignancy. This is in contrast to Maiduguri and Sokoto in Northern Nigeria where it is the fourth most common genital malignancy [7, 8].

By virtue of their high vascularity and the affinity of the trophoblast for blood vessels, metastasis occurs early via the blood stream [4]. The most

common site of such metastasis is the lungs which may be in form of pleural effusion, hemothorax or pleural seedlings [4]. It may also metastasize to genital structures and other distance structures such as the kidneys, liver and brain among other structures. The presenting symptoms of choriocarcinoma depend on the organ(s) involved in invasion and therefore is a great imitator of a wide variety of diseases [9].

The International Federation of Gynaecologists and Obstetrics classified choriocarcinoma based on their anatomic site into four stages. In stage I, it is confined to the Uterus while in stage II, it has spread to other genital structures; stage III is the metastasis to the lungs while stag IV has to do with other distance metastasis. On the other hand, the modified WHO prognostic scoring system using 8 risk factors reliably predicts the potential response to chemotherapy. It is categorized into low risk or high risk which responds poorly to chemotherapy.

Surprisingly choriocarcinoma is highly chemo-sensitive and therefore curable with 100% cure for cases without metastasis and 65-90% cure for patients with metastatic disease [2]. Its diagnosis as well as monitoring and follow up, has been made easy. This is because it elaborates human chorionic gonadotrophin which is readily assayed in blood or urine. Despite all the promising prognosis, the management and outcome of treatment of choriocarcinoma has not been studied in Sokoto. This has necessitated this review.

MATERIALS AND METHOD

This was a 5 – year retrospective descriptive study. Case notes of patients diagnosed with choriocarcinoma, from January 1st 2008 to December 31st 2012, at Usmanu Danfodiyo University Teaching Hospital, Sokoto, were retrieved manually from the health records department. Data relating to age, parity, presentation, predisposing factors, cost of treatment, morbidity and mortality were extracted and analyzed using the SPSS for windows version 16.0. Results are tabulated in frequency and percentages. Ethical approval for the study was from the Hospital Ethics Committee.

RESULTS AND DISCUSSION

There were 24 cases of choriocarcinoma giving an incidence of 1.5 per 1000 deliveries. Twenty-one case files were retrieved which had complete information for analysis giving a retrieval rate of 87.5%.

The ages of the patients ranged between 19 to 50 years with a mean of 33.21 ± 2.14 years. Most (61.9%) were grand multipara and (90.5%) were not gainfully employed. Majority were of the Hausa ethnic group (Table-1).

Table-1: **Socio-demographic characteristics of the patients**

Characteristic	Frequency	Percentage
Age		
15 – 24	4	19.1
25 – 34	4	19.0
35 – 44	11	52.4
≥ 45	2	9.6
Occupation		
Skilled Job	1	4.8
Unskilled Job	1	4.8
Unemployed	19	90.5
Tribe		
Fulani	2	9.5
Hausa	19	90.5
Others	0	0

Majority (61.9%) paid out of pocket fee for treatment of about Two hundred thousand (₦200,000.00) Naira ($600) (Table-2).

Table-2: Cost of treatment

Cost of treatment	Frequency	%
≤₦200,000	8	38.1
≥₦200,000	13	61.9
Total	21	100.0

A large number of the patients (33.3%) signed and left the hospital against medical advice (SAMA).

Majority of patients who had treatment were on admission for over 100 days (52.4%) while those that stayed less than 50 days on admission were those that signed against medical advice or who died while on admission (Table-3).

Table-3: Days in hospital

Hospital Stay	Frequency	%
≤100 days	10	47.6
≥ 100 days	11	52.4
Total	21	100.0

The common presenting complaints were recurrent vaginal bleeding (95.2%), passage of vesicles/foul smelling vaginal discharge (57.1%) and repeat MVA (47.9%). About 90.5% of the patients needed blood transfusion (Table-4).

Table-4: Clinical presentation

Symptoms	Frequency	%
Recurrent vaginal bleeding	20	95.2
Passage of vesicle or foul-smelling vaginal discharge	12	57.1
Repeated MVA	9	42.9
Exaggerated pregnancy symptoms or weight loss	8	38.1
Misdiagnosed	2	9.5
Sub-urethral nodule or vaginal mass	8	38.1
Theca lutein cyst of 1 or 2 ovaries	2	9.5

The most common antecedent pregnancy that preceded the choriocarcinoma in this study was complete mole (47.6%) followed by spontaneous abortion (28.6%).

Table-5: Antecedent Pregnancy preceding choriocarcinoma

Antecedent Pregnancy	Frequency	Percent
Spontaneous abortion	6	28.6
Complete Mole	10	47.6
Partial Mole	1	4.8
Term pregnancy	2	9.5
Unknown	2	9.5
Total	21	100.0

Majority (57.1%) were diagnosed 6 months after the antecedent event. Five, (23.8%) had non metastatic (FIGO Stage I) cancer while in 16 (76.2%) the cancer had metastasized. The common sites of metastasis were the vagina/pelvic structures (47.6%), uterus/cervix (42.9%) and lungs (33.3%) (Table-6).

Table-6: Sites of metastasis

Sites of Metastasis	Frequency	Percentage
vagina and pelvic structures	10	47.6
local - uterus, cervix	9	42.9
Lungs	7	33.3
liver, brain, pancreas	5	23.8

The diagnosis of choriocarcinoma was mainly by a combination of clinical, ultrasound and biochemical tests in 52.6% patients. About 90.5% of the patients had β-hCG levels greater than 10,000 mIU/ml at diagnosis.

Majority (57.1%) had combination chemotherapy in the form of Methotrexate, Actinomycin-D and Cyclophosphamide while methotrexate alone or MAC constituted 61.9% in most cases of which treatment was changed to alternate treatment due to disease progression (Table-7).

Table-7: Type of treatment offered to women with choriocarcinoma in UDUTH

Mode of treatment	Frequency	Percent
ANTIKOCKS	1	4.8
EMACO+HYST	1	4.8
MAC	6	28.6
MAC+HYST>EMACO	1	4.8
MAC> EMAC	1	4.8
MAC>EMACO	2	9.5
MAC>EMACO+HYST>	1	4.8
MAC>EMACO>EMACE	1	4.8
Methotrexate	1	4.8
NIL	1	4.8
SAMA	5	23.8
Total	21	100.0

Majority (52.4%) had no form of follow-up as they signed against medical advice and left the hospital or were lost to follow up.

The common complications encountered during the treatment were progression of the disease despite treatment in 33.3% and myelosuppression (33.3%). Others were mucositis (28.6%) and elevated liver enzymes (28.6%).

Table-8: Complications encountered during treatment

Complications	Frequency (n=21)	Percentage
Myelosuppression	7	33.3
Disease progression/recurrence	7	33.3
GIT- mucositis	6	28.6
Elevated liver enzymes	6	28.6
Alopecia	4	19.0
No record or no complication	4	19.0
Thrombophlebitis and tissue necrosis	2	9.5
Hyperpigmentation	1	4.8

Only 3 (14.3%) of the patients in the years under review were alive at the time of this review. The five-year survival rate was 9.5%. Majority of the patients (58.3%) who underwent treatment, and whose diagnosis – death interval could be determined died within 12 months of presentation.

The incidence of choriocarcinoma in Usmanu Danfodiyo University Teaching Hospital Sokoto was 1.5 per 1000 deliveries in the years reviewed. This is lower than the 4.4 per 1000 deliveries in Enugu [10] but similar to 1 in 1039 deliveries in Zaria, both in Nigeria [11].

The age of the mothers ranged between 19 and 50 years with a mode of 40 years which agrees with other studies that reported that the disease was 5-15 times higher in women 40 years and above [10, 12]. The mean age of occurrence was 33.21 ± 2.14 years which is similar to 33.6 years and 30.6 years reported in Enugu and Port Harcourt in Nigeria respectively [10, 13]. This study also showed that this condition was more common in the 4th decade of life as was also found in Enugu [10]. This is in contrast to findings in Zaria where it was more common in the 3rd decade of life and majority (76.2%) of the women were 20 years or below and 35 years or more [14]. Consequently extremes of age was one of the risk factors identified in these women. The high incidence of choriocarcinoma with advancing maternal age observed in this study may be related to the decreasing qualities of the ovum. Moreover, because as high as 61.9% of these women were grand multiparous, it pre-supposes that choriocarcinoma could have been prevented had these women used contraception.

Most of the women (90.5%) were not gainfully employed. This agrees with earlier studies that indicated that choriocarcinoma was common in women of low socioeconomic class and is probably related to nutrition [12].

The most common predisposing factor to choriocarcinoma found in this study was complete mole accounting for 47.6% of cases followed by spontaneous abortion (28.6%). This agrees with other studies [5, 15]. However, it is diverse from other studies majority of the choriocarcinoma were preceded by full term pregnancy and abortion respectively with molar pregnancy being least [10, 13]. A large scale multi-centred prospective study will therefore be required to determine the true risk factor(s) of choriocarcinoma in Nigeria.

Majority (57.1%) of the cases were diagnosed 6 months after the antecedent event probably because of late presentation which is a common problem in sub-Saharan Africa.

The common presenting complaints were recurrent vaginal bleeding (95.2%), passage of vesicles/foul smelling vaginal discharge (57.1%) and repeat manual vacuum aspiration (42.9%) for supposed incomplete evacuation. It therefore follows that any woman in the reproductive age group who presents with a history of recurrent/abnormal vaginal bleeding with or without passage of vesicles and/or repeat MVA, should be investigated to rule out choriocarcinoma.

Majority, (90.5%) needed blood transfusion with 10 units of blood being the median number of units transfused. This need for transfusion is as a result of a combination of factors; haemorrhage from the tumour, anaemia due to malignancy and the myelosuppressive effect of the cytotoxic drug used for its treatment.

The most common site of metastasis was the vagina/pelvic structures including the sub-urethral (47.6%) area. This was followed by the uterus (42.9%) and the lungs (33.3%). This finding is similar to the study in Port Harcourt [15].

The common modes of diagnosis were clinical (100%) and biochemical tests (81.0%) while a combination of clinical, ultrasound and biochemical tests was used in 52.6% of the patients. Both urine and serum β-hCG quantification was used suggesting an improvement in laboratory and health care deliveries in some tertiary centres in Nigeria as opposed to earlier reports from Enugu, Ilorin and some parts of Northern Nigeria [10, 16, 17]. About 85.7% of the women had β-hCG values greater than 10,000 mIU per ml at diagnosis which placed them as high risk.

As many as 33.3% signed against medical advice and left the hospital. This may be due to the level of poverty in our sub-region. It may also be the

reason for majority presenting late and hence with advanced disease.

The first line chemotherapy for treatment of choriocarcinoma during the period under review was methotrexate or MAC combination in 61.9% of patients and the commonly encountered complications were the progression of disease despite the treatment and myelosuppression. It therefore appears that methotrexate and MAC combination therapy as first-line treatment or sole treatment have not been adequate.

Although most of the patients were not gainfully employed, majority (61.9%) had over ₦200,000.00 ($600) spent out-of-pocket on their treatment. This could be the reason many of the patients (33.3%) signed and left against medical advice (SAMA). This underscores the need for a comprehensive health insurance scheme that caters for people of all works of life and not civil servants only.

Majority, 52.4% had no form of follow up and 36.8% were lost to follow up. More so, the 5 years survival was only 9.5%. This high case fatality, similar to findings in Enugu [10] is very dismal as what is globally expected and obtainable is 70-100%. The reasons for this have already been high-lighted above however, the contribution to late presentation and poor availability of drugs with affectation of timing of administration of drugs as earlier reported cannot be completely overlooked [18].

Some of the limitations of this study are its retrospective nature with attendant dependence on case notes as well as the high percentage of signing against medical advice (SAMA) and high absence of follow up. Both SAMA and inadequate follow up are major problems posing a threat to health care delivery in Sokoto and other parts of Nigeria [19]. However, this study is meant to stimulate prospective studies on the same theme.

CONCLUSION

The prevalence of choriocarcinoma in North Western Nigeria is low. However, it is selectively higher among older, grand multiparous women of low socioeconomic class. The cost of treatment was out of reach of many of them hence the high rate of abandoning treatment. The use of methotrexate and MAC regimen as first-line chemotherapy appeared to be ineffective and the five-year survival rate was only 9.5%.

RECOMMENDATIONS

The review of our local protocol to higher combination chemotherapy such as EMACO (Etoposide, Methotrexate, Actinomycin-D, Cyclophosphamide and Oncovin) is recommended especially in metastatic or high risk choriocarcinoma. Greater efforts should be made in the campaign for increased contraceptive uptake, as contraception may be useful in preventing choriocarcinoma in Sokoto. Finally, because the management of choriocarcinoma is capital intensive, assistance from government, philanthropist and non-governmental agencies will go a long way to achieve the 70-100% cure rate obtainable in developed countries.

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