CLINICAL AND HISTOPATHOLOGICAL PATTERNS OF OVARIAN MALIGNANCY IN THE UNIVERSITY OF PORT HARCOURT TEACHING HOSPITAL.

Bassey G, Nyengidiki T.K., Inimgba N.M., Otoide A.

Department Of Obstetrics And Gynaecology, University Of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.

CORRESPONDENCE:
EMAIL: *basseygoddy@yahoo.com*
PHONE: +234 803 70 290 78

ABSTRACT

Background:

Ovarian malignancy is the second commonest gynaecological malignancy in Nigeria and the leading cause of death from gynaecological cancers world-wide.

Objectives:

This study was to determine the prevalence and outcome of management of ovarian malignancies in the University of Port-Harcourt Teaching Hospital.

Methods:

This was a retrospective review of all cases of histologically confirmed ovarian malignancies managed in the University of Port-Harcourt Teaching Hospital over a 5-year period.

Results:

The prevalence of ovarian malignancy was 18.74/1000 gynaecological admissions and 10.93% of gynaecological malignancies. The mean age of patients was 44.32 years and the peak age of the disease was between 31 and 40 years. The most identifiable risk factor was late menopause in 5.9% of cases. The most frequent presenting symptoms were abdominal distention (94.1%) and abdominal pain (91.2%). Advanced disease was seen in 73.5% of cases. Most (76.0%) patients with advanced disease had duration of symptoms for a year or less. Epithelial cancers constituted 91.2% of cases and serous cystadenocarcinoma was the most frequent subtype. The case fatality rate was 5.9%. None of the surgeries was performed by a certified gynaecological oncologist. All patients were lost to follow up within one year of treatment.

Conclusion:

Epithelial ovarian cancers were the most commonly seen ovarian cancers in Port Harcourt. Advanced disease and poor compliance to chemotherapy were the norm amongst patients. More emphasis should be placed on prevention rather than screening. There is a pressing need for sub-specialization in gynaecological oncology.

Key words: Ovarian malignancy, management outcome, Port Harcourt.

INTRODUCTION

Ovarian malignancy is the second commonest gynaecological malignancy in Nigeria and the leading cause of death from gynaecological cancers world-wide.[1-5.] Sanni et al in 2013 in a 5

year retrospective study found an incidence rate for ovarian malignancy of 1 in 6.5 cases of gynaecological cancers, second only to cervical cancer.[3] It arises mainly from the epithelium and occasionally from the stroma or germ cells of the ovaries.[2] Recent evidence suggests that a large proportion of these tumours may arise from the fallopian tubes; spread and implant on the ovarian epithelium due to their close anatomical proximity.[1,2,5]

A woman has a 1-in-48 chance of developing ovarian malignancy in her life time[1]. The incidence is 1.4 in 100,000 women under 40 years of age increasing to 45 in 100,000 for women over 60 years of age[3]. The peak age is between 50 -70 years with a median age at diagnosis of 61 years.[1,6]. The overall five year survival rate is 46%, however this rate varies widely with the stage and grade of the cancer as well as the age of the patient at the time of diagnosis.[6]

The aetiology of ovarian malignancies is yet unknown but has been linked to incessant ovulation. Predisposing factors include use of ovulation induction agents, nulliparity, early menarche, late menopause, history of infertility, family history of ovarian malignancy, breast or colorectal cancers while combined oral contraceptive pills (COCP), multiparity, breastfeeding, anovulatory cycles and bilateral tubal ligation are protective.[1,2,6,7].

Ovarian malignancy presents with non-specific symptoms such as abdominal bloating, dyspepsia, easy satiety, nausea and constipation[1,2,7,8]. These are the minor signs of the disease and they are often over-looked by the patients and the physician. If these symptoms occur more than 12 times within a one-month period, possibility of ovarian malignancy should be entertained.[8] Patients with advanced disease commonly present with symptoms such as abdominal mass/swelling, ascites, back pain, abnormal vaginal bleeding and involuntary weight loss.[9-11].

Making a diagnosis of ovarian malignancy in the early stage of the disease from the history is difficult because of the non-specific symptoms of the disease.[1,2,11]. Pelvic examination finding of an adnexal mass, elevated tumour markers like Cancer antigen-125 (CA-125) and transvaginal ultrasonographic findings of a ruptured capsule, papillary excrescences and ascites are suggestive but not confirmatory.[1,6,11]. The risk of malignancy index was devised in an attempt to improve the sensitivity and specificity of diagnosing ovarian malignancy[12]. This scoring system takes into account the menopausal state, absolute value of CA-125 and ultrasonographic features as stated above. It has better sensitivity (74-88%) and specificity (74-92%) than the use of either CA-125 and ultrasonographic features alone[6,7,12,13,14]. These methods of screening are expensive, not 100% reliable and therefore not universally recommended.[1,2,12]. Due to lack of effective screening methods and non-specific early warning signs patients mostly present with advance disease leading to poor prognosis.[6]

Histology is the hallmark of making a diagnosis and a staging laparotomy or laparoscopy is required for all cases of suspected ovarian malignancy in order to obtain tissue for histopathologic analysis and to determine the stage of the disease[6,11,13,14]. Total abdominal hysterectomy, bilateral salpingo-ophorectomy, partial omentectomy and peritoneal wash-out are integral part of the staging laparotomy especially in advanced cases. Epithelial ovarian tumours are the most common histological types of ovarian malignancies and include the serous epithelial tumours, mucinous tumours, endometriod tumors, clear cell tumours, Brenner tumours and mixed epithelial tumours. Sex cord tumuors include the granulosa cell tumours, granulosa-theca cell tumours, sertoli-leydig's cell tumours, and steroid cell tumours.[1,2,6] Following surgery, six courses of chemotherapy with a taxane (paclitaxel, docetaxel) and a platinum drug (cisplatin, carboplatin) is usually administered for residual disease[13].

The objective of this study was to determine the incidence, socio-demographic characteristics, clinical characteristics, surgical staging, histopathological serotype and outcome of management of ovarian malignancies in the University of Port-Harcourt Teaching Hospital, in other to make recommendations with a view of improving outcome

MATERIALS AND METHODS

This was a retrospective study of all cases of histologically diagnosed ovarian malignancy managed in the University of Port-Harcourt Teaching Hospital from the 1st of January 2008 to the 31st of December 2012. There were 106 suspected cases of suspected ovarian malignancy identified from the admission records within the study period. Of these, 85 patients' case records were retrieved and studied giving a retrieval rate of 90.1%. Thirty-four (34) patients had histologically confirmed ovarian malignancy and these formed the study group.

Permission was obtained from the heads of the department of Obstetrics/Gynaecology and medical records for the use of patient records for the conduct of this study. The folder numbers of patients who had ovarian malignancy were obtained from the gynaecological ward and theatre records. The folder numbers were then used to trace the case files of the patient from the medical records department and relevant data were extracted from the case files. The data extracted include age, occupation, educational level, marital status, religion, parity, menopausal state, known risk factors, clinical presentation, findings at surgery, stage of the disease, histological type as described by the histopathology department of the University of Port-Harcourt Teaching Hospital and management outcomes. Patient with secondary ovarian malignancy from metastatic disease were excluded from the study population The data was entered and analyzed using the

SPSS 17.0 (IBM, Armonk, NY USA). The results obtained were represented in percentages, means, bar charts, pie chart and frequency tables.

RESULTS

There were 1,814 gynaecological admissions during the study period and 311 of these admissions were for gynaecological malignancies. There were 106 suspected cases of suspected ovarian malignancy. However, thirty-four patients had histologically confirmed ovarian malignancy giving a prevalence of 18.74 per 1000 gynaecological admissions and 10.93% of gynaecological malignancies over the study period.

The mean age of patients was 44.32 years with a range of 18 – 86 years. The peak age of the disease was between 31 and 40 years (31.6% of cases). Patient between the ages of 15-45 years (reproductive age group) made up 61.7% (21) of the study population. Most of the patients had secondary level of education (42.1%). One out of the three patients with no formal education had early stage disease while 8 out of the 31 patients with some form of education had early stage disease and the difference was not statistically significant (p= 0.6156, OR=1.44). Being educated did not influence the stage of the disease. The parity of the study population ranged from 0-10 and grand-multiparity accounted for 36.8% and nulliparity accounted for 31.6%. Table 1 shows the sociodemographic characteristics of the patients.

Thirteen (38.2%) were Post-menopausal and two (5.9%) of these patients had a history of late menopause (after 52 years). Combined oral contraceptive pills had been used in the past for less than a year in 3 (8.8%) patients. Smoking was a risk factor identified in one patient (2.9%). Risk factors were not identified in 21 (61.8%) of the patients and none of the patients was obese or had a known family history of ovarian or any other cancers.

Most frequent presenting symptoms were abdominal distention in 32 (94.1%), abdominal pain in 31 (91.2%), ascites in 27 (79.4%), weight loss in 22 (64.7%) and anaemia 18 (52.9%) patients. Massive ascites ranging from 5-15 litres with resultant respiratory distress was seen in 5 (26.3%) patients. Abnormal uterine bleeding was observed in two cases (10.5%), these were the patients who presented with sex cord stromal cancers. Table 2 shows the clinical presentation of the patients with ovarian cancer

Epithelial cancers were found in 91.2% (31), sex cord stroma tumours accounted for 5.9% (2) while germ cell cancers were found in 2.9% (1) of patients. Serous cystadenocarcinoma was the most frequent (35.3%) form of epithelial tumours seen. Table 3 shows the various subtypes of ovarian malignancy seen in UPTH.

Symptoms had lasted for a year or less before diagnosis in 24 (70.6%) cases and more than one year in 10 (29.4%) cases. Thirty-four patients had staging laparotomy with or without cytoreduction for advanced disease. Nine (26.5%) patients had early stage disease (stages 1 and 2) while 25 (73.5%) patients had advanced disease (stages 3 and 4). Nineteen (76.0%) of the 25 patients with advanced disease presented with duration of symptoms of one year or less while 5 (55.5%) of the 9 patients with early stage disease presented with duration of symptoms for a year or less and the difference was not statistically significant ($p= 0.229$, $OR= 2.53$). However, patients with duration of symptoms for a year or less were twice more likely to present with advance disease. Table 4 shows duration of symptoms and stage of the disease.

None of the surgeries was performed by certified gynaecological oncologist. Twenty-two patients (64.7%) were lost to follow up before commencement of chemotherapy while 12 patients (35.3%) received adjuvant chemotherapy following surgery; six patients (17.6%)

completed the six courses of chemotherapy, two patients died during the course of treatment giving a case fatality rate of 5.9% while four patient were lost to follow up after 1-3 courses of chemotherapy. All the patients were lost to follow up within one year post-surgery.

Table 1 - Sociodemographic Data Of Patients In The Study Group

AGE (YEARS)	FREQUENCY	PERCENTAGE (%)
≤ 20	1	2.9
21 – 30	4	11.8
31- 40	11	32.4
41 – 50	7	20.6
51 – 60	6	17.6
≥61	5	14.7
PARITY		
0	11	32.4
1	4	11.8
2-4	7	20.6
≥5	12	35.3
EDUCATIONAL STATUS		
None	3	8.8
Primary	6	17.6
Secondary	13	38.2
Tertiary	12	35.3

Table 2 – Clinical Presentation

Presentation	Frequency	Percentage (%)
Abdominal distention	32	94.1
Abdominal pain	31	91.2
Ascites	27	79.4.
Weight loss	22	64.7
Anaemia	18	52.9
Respiratory difficulty	5	14.7

Table 3 – Histological types

Histology type	Frequency	Percentage (%)
Epithelial tumours	31	91.2
-Serous adenocarcinoma	12	35.3
-Adenocarcinoma	8	23.5
- Mucinous cystadenocarcinoma	7	20.6
-Endometroid cell tumour	2	5.9
-Squamous cell carcinoma	2	5.9
Sex cord stroma tumour	2	5.9
-Granulosa cell tumour	2	5.9
Germ cell tumour	1	2.9
-Immature teratoma	1	2.9

Table 4 - Duration Of Symptoms And Stage Of The Disease.

Duration (months)	Frequency	Percentage (%)
≤ 12	24	70.6.
13 – 24	4	11.8
25 – 36	2	5.9
37- 48	1	2.9
>48	3	8.8
Stage		
1	3	8.8
2	6	17.6
3	16	47.1
4	9	26.5

DISCUSSION

The prevalence of histologically diagnosed ovarian malignancy from this study was 18.74 per 1000 and it accounted for 10.93% of all gynaecological malignancies during the study period. This corresponds to the incidence of 1.5% reported in a similar study in Ibadan.[15] It is lower than that reported in Ilorin, Uyo and Benin[16-18] but higher than the incidence of 1 in 405 gynaecological admissions reported in Enugu[19] where patients without a histologic diagnosis of ovarian malignancy were also excluded from the study.

Patients presenting with ovarian malignancy in this study were younger than reported for the developed world.[1,7] The peak age of incidence was 31-40 years, with a mean age of 45.74 years. Worthy of note, is the fact that 61.7% of patient with ovarian malignancy in this study were within the reproductive age group. This is really a cause for concern as the disease is seen to affect young women at the prime of their reproductive carrier. A previous study done in the University of Port-Harcourt Teaching Hospital by Nwosu et al[20] to determine the relative frequencies of gynaecological malignancy reported a peak age of incidence of 40.4 years. This is similar to reports from studies carried out in Benin, Ibadan and Uyo.[15,17,18] Most patients affected were multiparous and this finding was also collaborated by the study in Enugu.[19] Contrary to known patterns of the disease, young age and multiparous patients were most affected in this study[1,6,7]. It is likely that other risk factors at variance with risk factors in developed nations may be responsible for ovarian malignancy in our environment and this calls for further studies.

The known risk factors identified in the study population were; late menopause in 5.9% (2) and smoking in 2.9% (1) of cases. More than half of the patients in this study (61.8.%) had no identifiable known risk factors. It is therefore important that doctors have a high index of suspicion when a patient presents with recurrent gastrointestinal symptoms. Once ovarian malignancy has been included in the list of diagnostic possibilities, a pelvic examination, CA-

125, transvaginal ultrasound scan should be conducted with the aim of identifying early stage disease. However, these investigations on their own have a low sensitivity and specificity for the disease[12]. As emphasized earlier, using a combination of CA-125, transvaginal ultrasound findings and the menopausal state of the patient in a scoring system called the risk of malignancy index has a positive predictive value of 71.3%[12]. Patient with score of 250 is strongly suggestive of ovarian malignancy and should be further evaluated[12]. These investigations, however, are expensive and not always available in low resource settings. As such, patients with suspected ovarian malignancy should be referred to higher facilities where screening and/or diagnostic tests can be done.

Most of the patients presented with symptoms suggestive of advance disease and no patient presented with early warning signs or minor symptoms. This is akin to findings in Lagos, Ibadan, Benin, Maiduguri, Karachi (Pakistan) and Poland.[11,13,18,21-24] In a study conducted at the department of Gynaecology and Obstetrics, Liaquat National Hospital, Karachi from 2003 to 2007, involving 75 patients, more than half of the study population (56%) had stage III and IV disease[11]. Iyoke et al in a retrospective longitudinal analysis of the presentation and treatment of histologically diagnosed primary gynecological cancers from 2000 to 2010 in a tertiary hospital in South-East Nigeria also noted that 76% of patients with ovarian malignancy had advanced disease requiring debulking surgery as the main stay of treatment followed by adjuvant chemotherapy[19]. Most Patients with advanced disease had duration of symptoms for less than a year. This depicts the aggressive nature of ovarian tumours and underscores the importance of prevention over screening which has not been shown to be reliable. At present the most reliable preventive tool available is the use of COCP which reduces the risk of ovarian malignancy[1,2,6]. This may be difficult to implement amongst the study population with a high proportion of

nulliparous women within the reproductive age group in a society where child bearing is of utmost importance. There is therefore the need to develop more effective and practicable preventive measures for ovarian cancer that will address the peculiarity of the study population.

Epithelial ovarian cancers were the commonest type of ovarian malignancies, constituting 91.2% of cases. This is consistent with results from similar studies from different regions in Nigeria and around the world. It constituted 76.2% of cases in Ibadan, 68% of cases in Enugu, 73.8% of cases in Benin, 43.9% of cases in Ilorin and 90% of cases in Pakistan.[15-19,21,24] Advanced disease was seen in 87.5% of cases in this study, 84.5% of cases in Enugu[19], 81% of cases in Ibadan[15], 76.2% of cases in Benin[18], 72% of cases in Poland[11] and 56% of cases in Pakistan[24]. The two patients who had sex-cord stromal ovarian cancers presented with abnormal uterine bleeding which may have occurred due to oestrogen expression from granulosa cell tumours. The patient who had germ cell ovarian disease was an 18 year old with stage 2 disease. These three patients were lost to follow up and so the prognosis of their sub-type of cancer could not be assessed in this study.

There was poor compliance with adjuvant chemotherapy as experienced in other studies across Nigeria.[15,18,19,22,23] Patients in this study were not adequately followed up, so the case fatality rate and 5-year survival rate could not be accurately ascertained. There is need for further study into the reasons for poor treatment compliance in this centre.

The study is limited on account of poor case follow up, the small sample size which may not be a true representation of ovarian malignancy in Port Harcourt and being a retrospective study reduces the power of the study.

CONCLUSION

Women of reproductive age and grandmultiparous women were most affected by the disease in this study. Late presentation with advanced disease and poor compliance with chemotherapy were the norm amongst patients. More emphasis should be placed on prevention rather than screening. Provision of specialized and subsidized oncology care may result in better outcomes.

Conflict of interest : Nil

REFERENCES

1. Gabra H. Epithelial ovarian cancer. In: Edmonds KD (ed). *Dewhurst's Textbook of Obstetrics & Gynaecology. 7th edition. London, Blackwell Publishing, 2007*; 625-35.
2. Ola ER. Tumours of the ovary. In: Akin Agboola (ed). *Textbook of Obstetrics and Gynaecology for Medical Students. 2nd edition, Ibadan, Heinemann educational books, 2006*; 197-217.
3. Sanni WO, Ocheke AN, Oyebode T, Jonah M, Nyango DD, Silas OA, Sagay AS. Pattern of Gynaecological Malignancies in Jos. *Tropical Journal of Obstetrics and Gynaecology, April 2013*; 30 (1): 97-102.
4. Olakanmi RA, Adekoyejo AP, Olubanji AO, Olatunji MA. Cancer Mortality Pattern in Lagos University Teaching Hospital, Lagos, Nigeria. *Journal of Cancer Epidemiology, 2015* , Article ID 842032.
5. Erickson BK, Conner MG, Landen CN (Jr). The role of the fallopian tube in the origin of ovarian cancer. *American Journal of Obstetrics and Gynecology. 2013 Nov*; 209(5): 409-414.
6. Cancer.Net Editorial Board; Ovarian Cancer – Statistics. Cancer.net Articles, *American Society of Clinical Oncology (ASCO) – Cancer.Net, 2012*. http://www.cancer.net/cancer-types/ovarian-cancer/statistics. Accessed 10/4/2016
7. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Ovarian cancer and oral contraceptives: collaborative re-analysis of data from 45 epidemiological studies including 23, 257 women with ovarian cancer and 87, 303 controls. *The Lancet. 2008*; 371(9609): 303-14.

8. Lurie G, Thompson PJ, McDuffie KE, Carney ME. Goodman MT. Pre-diagnostic symptoms of ovarian carcinoma: a case-control study. *Gynecology Oncologist. 2009*; 114(2): 231-6.
9. Webb PM, Purdie DM, Grover S, Jordan S, Dick ML, Green AC. Symptoms and diagnosis of borderline, early and advanced epithelial ovarian cancer. *The Gynecology Oncologist. 2004*; 92(1): 232-9.
10. Friedman GD, Skilling JS, Udaltsova NV, Smith LH. Early symptoms of ovarian cancer: a case control study without recall bias. *Family Practice. 2005*; 22(5): 548-53.
11. Nowak M, Szpakowski M, Malinowski A, Wieczorek A, Szpakowski A et al. Ovarian cancer. I. Epidemiology, symptoms, FIGO staging. *Ginekol Pol.2000*; 71(9):1179-83.
12. Enakpene CA, Omigbodun AO, Goecke TW, Odukogbe A, Beckmann MW. Preoperative evaluation and triage of women with suspicious adnexal masses using risk of malignancy index. *J Obstet Gynaecol Res 2009*; 35(1):131-8.
13. Winter-Roach BA, Kitchener HC, Lawrie TA. Adjuvant (post-surgery) chemotherapy for early stage epithelial ovarian cancer. *Cochrane Database Systemic Review, 2012*; 14(3): CD0044706.
14. Elattar A, Bryant A, Winter-Roach BA, Hatem M, Naik R. Optimal primary surgical treatment for advanced epithelial ovarian cancer. *Cochrane Database Systemic Review, 2011*; (8): CD007565.
15. Odukogbe AA, Adebamowo CA, Ola B, Olayemi O, Oladdokun A, Adewole IF et al. Ovarian cancer in Ibadan: Characteristics and Management. *Journal of Obstetrics & Gynaecology. 2004*; 24(3): 294-7.

16. Buhari MO, Ojo BA, Ijaiya MA, Aboyeji PA. Ovarian Cancer in Ilorin, Nigeria: A Review of Over 80 Cases. *Nigerian Quarterly Journal of Hospital Medicine. 2005*; 15(3): 127-30.
17. Bassey EA, Ekpo MD, Abassiatai A. Female genital tract malignancies in Uyo, South-South Nigeria. *Nigerian Postgraduate Medical Journal. 2007*; 14(2):134-6.
18. Gharoro EP, Eirewele O. Cancer of the ovary at the University of Benin Teaching Hospital: a 10-year review, 1992-2001. *African Journal of Medicine and Medical Sciences. 2006*; 35(2):143-7.
19. Iyoke C, Ugwu G, Ezugwu E, Onah N, Ugwu O et al. Incidence, pattern and management of ovarian cancer at a tertiary medical center in Enugu, South East Nigeria. *Annals of Medical Health Sciences and Research. 2013*; 3(3): 417-21.
20. Nwosu SO, Anya SE. Malignancies of the female genital tract at the University of Port-Harcourt Teaching Hospital: a ten year review – 1990-1999. *Nigerian Postgraduate Medical Journal. 2004*; 11(2): 107-9.
21. Iyoka CA, Ugwu GO, Ezugwu EC, Ezugwu FO, Lawani OL et al. Challenges associated with the management of gynecological cancers in a tertiary hospital in South East Nigeria. *International Journal of Women's Health. 2014*; 24(24): 123-30.
22. Onyiaorah IV, Anunobi CC, Banjo AA, Fatima AA, Nwankwo KC. Histopathological patterns of ovarian tumours seen in Lagos University Teaching Hospital: a ten year retrospective study. *Nigerian Quarterly Journal of Hospital Medicine. 2011*:21(2): 114-8.
23. Kyari O, Nggada H, Mairiga A. Malignant tumours of the female genital tract in North eastern Nigeria. East African Medical Journal. 2004; 81(3): 142-5.

24. Khan A, Sultana K. Presenting signs and symptoms of ovarian cancer at a tertiary care hospital. *Journal of Pakistani Medical Association. 2010*; 60(4):260-2.