AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 34 NUMBER 3 SEPTEMBER 2005

ISSN 1116—4077

Afr. J. Med. med. Sci. (2005) 34, 307-309

Total ovulating period: any contribution to ovarian carcinogenesis?

AA Odukogbe, *CA Adebamowo, AO Adeniji, AO Omigbodun, O Olayemi,
A Oladokun, MS Owolabi, C Aimakhu, IF Adewole and **E. Owoaje

*Ovarian Cancer Service, Gynecological Oncology Unit, Departments of Obstetrics and Gynecology, *Surgery and **Community Medicine, College of Medicine/University College Hospital, University of Ibadan, Ibadan, Nigeria.*

Summary

The etiology of ovarian cancer has many postulates including that of incessant ovulation. Women of high parity especially those that breastfeed in addition are supposed to be protected. Ovarian cancer patients in the developing world are of higher parity than their Caucasian counterparts. Our study compared the length of reproductive career (LRC), the physiological ovulation free period (PFP) and the total ovulating period (TOP) amongst histologically proven ovarian cancer patients and age - matched controls. This is a questionnaire survey of 21 ovarian cancer patients managed by us between 1st December 1998 and 31st July 2002 and 42 gynaecological patients not known to have ovarian cancer. The mean age among the patients was 45.7±16.9 years while among the controls it was 45.4±16.1 years. The mean parity of the patients was 3.6±2.2 compared to 3.4±2.9 in the controls. The patients had a mean LRC of 23.8±11.2 years while in the controls it was 25.7±10.8 years. The mean PFP of the patients was 7.4±5.6 years and for the controls 7.1±6.5 years. The patients had a mean TOP of 15.8±8.8 years while this was 18.6±8.1 years for the controls. None of these differences was statistically significant. Our study revealed no statistically significant differences in the total ovulating periods between ovarian cancer patients and age - matched controls. Further studies will be necessary.

Keywords: *Ovarian cancer, total ovulating period, carcinogenesis*

Resume

L'etiologie du cancer ovarien a beaucoup de postulats qui incluent une ovulation incessante. Les femmes qui allaitent de plus doivent etre protégées contre la maladie. Les malades du cancer ovariens dans le monde en voie de development sont de plus grande parite que les cancariennes. Notre etude a comparer la longeur de la carriere reproductrice (LCR), l'ovulation de la periode libre physiologique (PLP) et la periode d'ovulation totale (POT), parmi les maladies du cancer ovarien qui ont ete confirmes histologiquement. C'est une etude des questionnaires de 21 malades du cancer ovarien que l'on a fait pendant la periode du 1, Decembre 1998-31 Juillet 2002. 42 malades gynecoloques n'avaient pas le cancer ovarien L'age moyen parmi les maladies etait 4,7+ 16,9 ans alors que parmi les controles, c'etait 45,4 4+16,1 ans. La parite moyenne des maladies etait 3,6 + 2,2 comparee a 3,4+2,0 dans les controles. Les malades avaient un LCR moyen de 23 23,8 + 11,8 + 11,2 ans alors que dans les controles, c'etait 25,5+ 10,8 ans. Le PLP moyen des malades etait 7,4+5,6 ans pour les controles 7,1 + 6.5 ans . Les malades avaient un POT moyen de 15,8 + 8,8 ans alors que c'etait 18,6 + 8, 1 ans pour les controles. Aucune de ces differences n'etait statistique considerable Notre etude n'a revele aucune difference statistiquement considerablement dans les periodes totales d'ovulation entre les malades du cancer ovarien et l'age a egale les controles. Des etudes supplementaires seront necessaries.

Introduction

Ovarian cancer is a lethal disease [1]. Amongst the gynaecological cancers it has the highest case fatality rates due largely to its late detection [2].

Many theories have been propounded for its etiology without any consensus yet. One of the earliest is that of incessant ovulation [3,4], popularized by Fathalla. The main thrust of this is that unabated ovulation causes recurrent breaches in the epithelium covering the ovary, which subsequently develops carcinogenesis. Recent modifications opine that conversely, progestagen induced epithelial cell apoptosis protects against epithelial ovarian cancer [5]. It is for this reason that women who are nulliparous or of low parity are thought to form the majority of ovarian cancer patients, being more exposed to these recurrent epithelial breaches. This indeed is the situation; as such women constitute the vast majority of cases from the Caucasian populations of the technologically advanced countries [6].

A logical conclusion then would be that women of high parity ought to be protected from ovarian cancer [5]. This protection should also include the period of breastfeeding of the child since this suppresses ovulation to some extent too [4,7].

In the resource poor countries with higher parity [8], and extended breastfeeding periods, ovarian cancer is not so common as in their resource rich counterparts. The reasons for this have not been clearly elucidated. Interest

Correspondence: Dr. A.A. Odukogbe, Ovarian Cancer Service, Gynaecology Oncology Unit, Department of Obstetrics and Gynaecology, College of Medicine, University of Ibadan, Nigeria. E-mail: akin tundeodukogbe@yahoo.com

Presented in part at the 4th International Conference on Cancer in Africa of the African Organization for Research and Training in Cancer (AORTIC) in Accra, Ghana. 6 - 10 October 2003.

ingly however, women with high parity constitute the majority of the cases seen in these less advanced countries. Apart from the above stated possible protection from high parity, other possibilities for these low rates are sociocultural and economic factors which hamper clinicosurgical identification of patients with ovarian cancer.

Based on these unclear situations, the Ovarian Cancer Service (The Service) of our hospital sought to determine the total ovulating periods of the patients it managed and to compare these with those of age-matched controls without ovarian cancer.

Materials and methods

All suspected cases of ovarian cancer admitted to the Gynecological wards of the University College Hospital, (UCH), Ibadan had a standardized questionnaire administered prior to surgery. Questions pertaining to age, reproductive and clinical histories were inquired about at this stage. Only cases confirmed at laparotomy or postmortem and subsequent histological examination had the second part of the questionnaire completed and were entered into the study. This present report concerns the patients seen between December 1st 1998 and July 31st 2002. There were twenty-one of such patients.

Definitions

- Length of reproductive career (LRC). This is the period in years from menarche to menopause (including surgically induced menopause). For the controls that are still menstruating, it is the period up to the time of recruitment into this study.
- Physiological ovulation free period (PFP). An estimate of the physiological ovulation free period in years for each patient is calculated thus: each viable pregnancy is assumed to have lasted for forty weeks (except if clearly stated). Each abortion is assumed to have lasted for fourteen weeks (except if this period is well known). The period of breastfeeding is calculated in weeks also. All these weeks are added for each patient and divided by 52 to give the PFP in years.
- Total ovulating period (TOP). This is the difference between the length of reproductive career and the physiological ovulation free period.

A comparison was then made with the estimates calculated for forty-two randomly selected age-matched gynecological patients not having ovarian cancer who were interviewed in person.

The data analysis was done using the Microsoft Excel package and statistical significance set at p values less than 0.05.

Results

Age

Two groups, 41 – 50 and 51 – 60 years age groups of both patients and controls formed the highest proportions of 23.8%. In both groups, women above 60 years of age formed only 14.3% while those aged twenty years or less formed 4.8%. The mean age among the patients was 45.7±16.9 years compared to 45.4±16.1 years among the controls.

Parity

Patients and controls that had five or more deliveries formed the highest percentages of 47.6% and 40.5% respectively. Nulliparous women constituted 19.0% and 30.9% of the patients and controls respectively. Of the ovarian cancer group, the mean parity was 3.6± 2.2 as opposed to 3.4±2.9 in the controls.

LRC

The patients had the highest proportion, 38.1% in those whose career spanned 20-29 years. The corresponding values in the control group were 38.1% and 30-39 years. Only one patient, a 14 year old, was still menstruating as at the time of this study. She had unilateral oophorectomy for yolk sac tumor in year 2001. The mean LRC for patients was 23.8±11.2 years while this was 25.7±10.8 years for the controls. This difference was not statistically significant (p = 0.6).

PFP

These periods in both groups were similar, except for those whose physiological ovulation free periods spanned between 0 – 5 years (23.8% of patients compared to 40.5% of the controls).

However, there was no statistical significance (p = 0.4) between the mean PFP of the patients (7.4 ± 5.6 years) and the controls (7.1 ± 6.5 years).

TOP

Interestingly the control group had longer total ovulating periods than the patient group. Eighty-one percent of the control group ovulated for 10 – 29 years compared with 47.6% in the patient group. This is shown in Table 1.

Table 1: Total ovulating period in ovarian cancer patients and controls without ovarian cancer.

	Patients		Controls	
Period (years)	Number	(%)	Number	(%)
0 – 9	5	23.8	5	11.9
10 – 19	7	33.3	17	40.5
20 – 29	3	14.3	17	40.5
30 – 39	2	9.5	2	4.8
Not stated	4	19.0	1	2.4
Total	21	100.0	42	100.0

However the proportion of those who ovulated for the longest period (30 – 39years) amongst the patients (9.5%) was double that of the controls (4.8%).The mean period amongst the patients was 15.8±8.8 years with the corresponding values in the controls being 18.6±8.1 years. The t-test was 0.7 while the p-value was 0.5. This difference was not statistically different.

Discussion

The mean total ovulating period amongst the controls is unexpectedly higher than that of the ovarian cancer patients in this study. This difference is not statistically significant, although the population sizes are small. Titus–Ernstoff *et al* in 2001 [6] also found an inconsistent association between menstrual and reproductive factors in relation to ovarian cancer risks and subtypes. It may indicate that factors other than incessant ovulation are more important in ovarian cancer etiopathogenesis in the developing world.

A hypothesis worthy of further elucidation could be the possibility of peripartal inoculation of talc particles that may be contained in the surgical gloves used in the repeated vaginal examinations done when these women are in labour. Talc had previously been identified in the likely aetiopathogenesis of ovarian cancer especially in women who apply talc – containing powder on their external genitalia. The presence of talc granulomas in the ovaries of patients who have never been previously operated has been documented and may be explained by the continuity of the introitus and peritoneal cavity through the endocervical, endometrial and tubal cavities [9]. Of course this hypothesis will not explain the etiological mechanism of the nonepithelial types. This merits further research, to prove this hypothesis and to seek explanation in the case of the nonepithelial ovarian cancer.

Fertility rates are declining in the developing world and with it the protection from ovarian cancer of the ovulation suppression of pregnancy and breastfeeding and the pregnancy related progestagen induced epithelial cell apoptosis may be lost.

Therefore timely institution of prophylactic measures such as the prolonged use of the oral contraceptive pills in women desiring contraception and opportunistic oophorectomy in women above forty years of age will seem appropriate here. Indeed Yen and associates [10] working in Taiwan have documented a rise in ovarian cancer incidence likely to have resulted from the decline in parity.

Acknowledgements

The University of Ibadan Senate Research Grant No. SRG/COM/2000/28B financed part of this work. We are grateful to Mrs. Seun Adeyemo for secretarial assistance.

References

1. Edmondson R. J. and Monaghan J. M. The Epidemiology of ovarian cancer. Int. J. Gynecol. Cancer 2001, 11, 423 – 429.
2. Anderiesz Cleola and Quinn Michael A. Screening for ovarian cancer. MJA 2003; 178 (12): 655 – 656.
3. Purdie DM, Bian CJ, Siskind V, Webb PM, Green AC. Ovulation and risk of epithelial ovarian cancer. Int. J. Cancer 2003 Mar 20; 104 (2): 228 – 232.
4. Siskind V, Green A, Bain C, Purdie D. Breastfeeding, menopause and epithelial ovarian cancer. Epidemiology. 1997 Mar; 8 (2): 188 – 191.
5. Whiteman DC, Siskind V, Purdie DM, Green AC. Timing of pregnancy and the risk of epithelial ovarian cancer. Cancer Epidemiol Biomarkers Prev. 2003 Jan; 12 (1): 42 – 46.
6. Titus – Ernstoff L, Perez K, Cramer DW, Harlow BL, Baron JA, Greenberg ER. Menstrual and reproductive factors in relation to ovarian cancer risk. Br. J. Cancer. 2001 Mar 2; 84 (5): 714 – 721.
7. Greggi S, Parazzini F, Paratore MP, Chatenoud L, Legge F, Mancuso S, La Vecchia C. Risk factors for ovarian cancer in central Italy. Gynecol. Oncol. 2000 Oct; 79(1): 50 – 54.
8. Salazar – Martinez E, Lazcano – Ponce EC, Gonzalez Lira – Lira G, Escudero De los Rios P, Salmeron – Castro J, Hernandez – Avial M. Reproductive factors of ovarian and endometrial cancer risk in a high fertility population in Mexico. Cancer Res. 1999 Aug 1: 59(15): 3658 – 3662.
9. Harlow BL, Cramer DW, Bell DA et al. Perineal exposure to talc and ovarian cancer risk. Obstet Gynecol 1992; 80: 19
10. Yen ML, Yen BL, Bai CH, Lin RS. Risk factors for ovarian cancer in Taiwan. A case control study in low incidence population. Gynecol. Oncol. 2003 May; 89(2): 318 – 324.

Received: 16/02/04
Accepted: 09/06/05