ORIGINAL ARTICLE

Parity and Epithelial Ovarian Tumours

FATIMAH ZAHRA

ABSTRACT

Objective: To see the parity distribution in women with epithelial ovarian tumours and find out if there has been a protective effect of increasing parity.
Design: A descriptive study.
Setting: Federal Government Services Hospital, Islamabad.
Patients and methods: This was a 2 year study carried out from January 2004 to December 2005. All patients above 19 years age who underwent laparotomy for a suspected ovarian tumour and whose histopathological report subsequently turned out to be of an epithelial ovarian tumour (n=62) were included in the study. Parity distribution in these patients was noted.
Results: Parity distribution was nullipara 16(26%), multipara 46(74%), Women with parity 1-4 were 27(44%) and with parity above 5 were 19(30%). In patients with ovarian carcinoma maximum patients had parity of 3 and 8.
Conclusion: It seems nulliparity is not a significant factor in the aetiology of both benign and malignant epithelial ovarian tumours and increasing parity has not been protective for women in our country.
Key words: Ovarian cancer, ovarian tumours, parity, nulliparity, epithelial tumours.

INTRODUCTION

Ovarian Cancer affects between 1 and 2% of women in the developed world. It is the most lethal Gynaecological malignancy having a mortality incidence ratio of 0.675. Variations in the rates of ovarian cancer around the world are less marked than for other gynaecological cancers[1]. Ovarian Carcinoma is the 3rd most common malignancy in Pakistan. It accounts for 18 to 23% of all female cancers and 34% of all gynaecological cancers in Pakistan[2,3].

About 80% of cancers are adenocarcinomas. They are rare before the age of 35 years but incidence increases with age to a peak in the 50 to 70 years old age group. Just under half occur in women aged 45 to 65 years[4]. Benign Epithelial tumours occur at a slightly younger age than their malignant counterparts. They are most common in women over 40 years[5].

Factors causing ovarian cancer are not known. Epithelial tumours are most frequently associated with nulliparity, an early menarche, a late age at menopause and a long estimated number of years of ovulation[6]. The proposed causal relationship between ovarian stimulation and neoplasia is based on three main hypotheses. Fathalla's incessant ovulation hypothesis is most widely accepted. It suggests that epithelial ovarian carcinoma results from repeated ovulations, where the cumulative effects of each minor trauma on the ovarian epithelium can lead to malignant transformation[7]. This proposes that the risk of ovarian cancer is directly proportional to the number of ovulatory cycles between the menarche and the menopause. The second hypothesis suggests that persistent exposure of the ovary to endogenous or exogenous gonadotrophins or in conjunction with secondarily elevated oestradiol concentrations, may be directly carcinogenic. In vitro studies have shown that gonadotrophins stimulate deoxyribonucleic acid (DNA) synthesis and proliferation in a number of ovarian cancer cell lines and also significantly increase protein kinase C activity in these tumours[8]. The third hypothesis relates to the production of chemical carcinogens within the local ovarian environment after stimulation with gonadotrophins and oestrogens. In stimulated granulosa cells the microsomal P450 cytochrome dependent hydroxylation systems can convert aromatic polycyclic hydrocarbons into reactive hypoxides. These can destroy follicular cells and cause malignant transformation by forming covalent bonds with proteins and DNA[9].

There is an association between infertility and ovarian cancer. The link appears to be strongest in women with unexplained infertility and in women who have not been able to become pregnant at all[10]. Decreasing risk with increasing number of full term pregnancies has been consistently shown in over a dozen case-controlled studies. In a US study, one child was associated with a 40% reduction in risk, two children with a 60% reduction in risk and five or more with an 80% reduction. Ovarian surface epithelial cell

---

Federal Government Services Hospital, Islamabad
Correspondence to Dr. Fatima Zahra, Address: H. 257, Circular Road, Pakistan Town ,Zone 5, Islamabad. Email: dr_f_zahra@hotmail.com Cell: 0333-5579245

apoptosis induced by pregnancy hormones may be the underlying protective mechanism[11].

Pakistani women are known to have a higher parity compared to western women. There is a recent trend towards reproducing a lesser number of children in our women. In view of the high morbidity and mortality associated with Epithelial Ovarian tumours, the purpose of this study was to see the distribution of parity in women diagnosed with epithelial ovarian tumours and to compare the frequencies of these tumours in nulliparous and multiparous women to find out whether a higher parity had really been protective in our women.

PATIENTS AND METHODS

This was a descriptive study conducted from January 2004 to December 2005 (2 years) at Federal Government Services Hospital, Islamabad. The inclusion criteria for this study was patients having asymptomatic echo-free ovarian cysts more than 7.9 cm in diameter, Asymptomatic ovarian cysts of any size that are not echo-free are multilocular or have septa, solid parts or papillary formations, Asymptomatic ovarian cysts of any size associated with raised serum CA-125 levels or symptomatic ovarian cysts of any size associated with symptoms like severe acute pain or signs of intraperitoneal bleeding or torsion. The exclusion criteria was patients having asymptomatic, simple, echo free, unilocular, unilateral ovarian cysts without solid parts or papillary formations, less than 8cm in diameter and normal CA-125 levels and females who were less than 19 years. All patients presenting from January 1, 2004 to December 31, 2005 who were 19 years of age and above (reproductive and menopausal age group) according to inclusion criteria underwent laparotomy after taking informed consent. Histopathology of the ovarian mass was done at the pathology department of Federal Government Services Hospital and women who turned out to have Epithelial ovarian tumours were included in the study. The histological characterization of the tumours was done according to the classification proposed by WHO. Patients were divided in three groups according to their parity. The three groups were Nullipara, Women with parity from 1 to 4 and women with parity of 5 and above. A proforma was designed to fill the relevant data about the patient. Data was analyzed by SPSS version 10.0. Frequencies and Percentages were calculated for each parity group and chi square test was applied to see the statistical significance of difference in frequencies of epithelial ovarian tumours between Nulliparous and Multiparous women at the level of .05 significance.

RESULTS

Sixty-two patients in the reproductive and menopausal age group (19 years and above) were diagnosed to have Epithelial ovarian tumours. Of the patients included in this study 9(15%) were menopausal and 53(85%) were in the reproductive age group. Benign Epithelial ovarian tumours were seen in 44(71%) and ovarian carcinoma was seen in 18(29%) of the patients. The different histological types of epithelial ovarian tumours seen were Mucinous cystadenomas 12(19%), Serous cystadenomas 32(51%), Mucinous cystadenocarcinoma 6(10%), Serous cystadenocarcinoma 8(13%), Endometrioid carcinoma 3(5%) and undifferentiated carcinoma 1(2%).

In patients suffering from epithelial ovarian tumours the distribution of parity was nullipara 16(26%), multipara 46(74%), 27(44%) had a parity of 1 to 4 and 19(30%) had a parity of more than 5. In patients suffering from benign epithelial tumours 12(27%) of the women were nulliparous while 32(73%) were multiparous. Parity of 1 to 4 was seen in 20(45%) while, 12(27%) had a parity of more than 5. In patients suffering from malignant epithelial tumours, 4(22%) were nulliparous, 14(78%) were multiparous, 7(39%) had a parity ranging 1 to 4 and a similar number of patients had a parity above five 7(39%).

Patients with a parity of 2 had the minimum percentage of benign epithelial tumours 1(3%) while patients with a parity of 4 had the maximum number of benign tumours 9(28%). No relationship of parity with the frequency of benign tumours is seen. In cases of ovarian carcinoma none of the patients had a parity of 4, while maximum number of patients with a parity of 3 and 8 were seen to suffer from ovarian carcinoma 3(22%) for each group. We had 9 patients in the menopausal age group, of these patients only 1(11%) was nulliparous while 8(89%) were grandmultipara having more than 4 children.

In our study 40 patients had serous ovarian tumours and 18 patients had Mucinous ovarian tumours. In patients suffering from Mucinous tumours the parity distribution was nullipara 3(17%), 6(33%) parity of 1-4, 9(50%) parity above 5. In patients diagnosed with Serous tumours 13(32%) were nullipara, 11(28%) were of parity 1-4 and 16(40%) had parity of 5 and above. In both histological types maximum number of patients had parity of 5 and above.

Surprisingly in both benign and malignant epithelial ovarian tumours maximum number of patients was seen in multipara compared to nullipara and increasing parity seemed to have no protective

effect. Instead, multipara was seen to have a worst prevalence of ovarian tumours.

DISCUSSION

Nulliparity is considered to be a risk factor for the development of ovarian carcinoma. Most of the western studies have shown that nulliparous women have high incidence of ovarian cancers. According to these studies multiparity was associated with a significant reduction in risk of ovarian cancer and the high risk of ovarian cancer is inversely related to the number of full term pregnancies and each additional sibling as associated with a risk reduction[12,13,14,15,16,17]. However, the majority of our patients diagnosed with epithelial ovarian tumours 46(74%) were multipara and a lesser number of patients turned out to be nulliparous. In patients suffering from ovarian carcinoma 14(78%) were multipara and 4(22%) were nullipara. In patients suffering from epithelial ovarian carcinoma 7(39%) had a parity of 1-4 and the same percentage 7(39%) had a parity of 5 and above.

Interestingly, the percentage of women with 5 or more children 7(39%) were greater than those who were nulliparous 4(22%). This finding shows no protective effect of increasing parity on the risk of epithelial ovarian carcinoma,

In the group of patients with benign epithelial ovarian tumours, a lesser number of patients were nullipara 12(27%) and majority was multipara 32(73%). The proportion of women who were nulliparous was almost same in patients with benign epithelial tumours (27%) and those with epithelial ovarian carcinoma (22%). This shows that the parity spectrum is similar for both benign and malignant epithelial ovarian tumours.

Our findings are similar to those observed in most earlier Pakistani studies carried out at Rawalpindi, Karachi and Lahore[18,19,20] and a study carried out at Ibadan(Nigeria)[21]. A study conducted by Nieto JJ et al did not find any evidence of a difference in dysplasia score between nulliparous women and controls neither before nor after adjusting for age[22].

CONCLUSION

It seems nulliparity is not a significant factor in the aetiology of both benign and malignant epithelial ovarian tumours and increasing parity has not been protective for women in our country.

REFERENCES

1. Sasiene P, Cuzick J. Epidemiology of gynaecological cancer. In: Shaw R, Soutter WP, Stanton S. Gynaecology. 3rd ed. Edinburgh: Elsevier Science; 2003. 677-98.
2. Jafarey NA, Zaide SHM. Cancer in Pakistan. J Pak Med Assoc 1987; 37: 178-83.
3. Baloch R, Abro H, Abassi SA. Ovarian carcinoma-local experience at Shaikh Zayed hospital for women (CMCH) and (LINAR) Larkana. Med Channel 2003; 9: 59-62.
4. Dina R, Rustin G, Soutter P. Carcinoma of the ovary and fallopian tube. In: Shaw R, Soutter WP, Stanton S. Gynecology. 3rd ed. Edinburgh: Elsevier Science, 2003: 677-98,
5. Soutter P, Girling J, Haidopoulos D. Benign tumors of the ovary. In: Shaw R, Soutter WP, Stanton S. Gynecology. 3rd ed. Edinburgh: Elsevier Science, 2003: 665-76. Hildreth NG, Kelsey JL, Livolsi VA. An epidemiological study of epithelial carcinoma of the ovary. Am J Obstet Gynecol 1981; 114: 389-405.
6. Hildreth NG, Kelsey JL, Livolsi VA. An epidemiological study of epithelial carcinoma of the ovary. Am J Obstet Gynecol 1981; 114: 389-405.
7. Fathalla MF. Incessant ovulation: a factor in ovarian neoplasia? Lancet 1971; 2: 163.
8. Nugent D, Salha O. Ovarian neoplasia and subfertility treatments RCOG 1998. Br J Obstet Gynaecol 1998; 105: 584-91.
9. Nash JP, Ozole RF, Smyth JF. Oestrogen and antioestrogen effects on the growth of human epithelial ovarian cancer in vitro. Obstet Gynecol 1989; 3: 1009-16.
10. Rodriguez GC, Berchuck A, Whitaker RS. Epidermal growth factor expression in normal ovarian epithelium and ovarian cancer. Am J Obstet Gynecol 1991; 164: 745-50.
11. Titus-Ernstoff L, Perez K, Cramer DW. Menstrual and reproductive factors in relation to ovarian cancer. Br J Cancer 2001; 84: 714-21.
12. Harlap S, Olson SH, Curtin JP, Caputo TA, Nakraseine C, Sanchez D, Xue X. Epithelial ovarian cancer and fertility of patients. Epidemiol 2000; 13: 59-65.
13. Chiaffaine F, Pelluchi C, Parazzini F, Negri E, Franceshi S, Talamini R et al. Reproductive and hormonal factors and ovarian cancer. Ann Oncol 2001; 12:337-41.
14. Greggi S, Parazzini F, Paratore MP, Chatenoud L, Legge F, Mancuso S et al. Risk factors for ovarian cancer in central Italy. Gynecol Oncol 2000; 79:50-4.
15. Salazar-Martinez E, Lazeano-Pance EC, Gonzalez Lira-Lira G, Escudero- De Los Rios P, Salmeron-Castro J, Hernandez-Avila M. Cancer Res 1999; 59:3658-62.
16. Yen ML, Yen BL, Bai CH, Lin RS. Risk factors for ovarian cancer in Taiwan: a case control study in a low incidence population. Gynecol Oncol 2003; 89: 318-24.
17. Zhang M, Lee AH, Binns CW. Reproductive and dietary risk factors for epithelial ovarian cancer in China. Gynecol Oncol 2004; 92: 320-6.
18. Jamal S, Malik A, Ahmad M, Mushtaq S, Khan AH. The pattern of malignant ovarian tumours –A study of 285 consecutive cases at the Armed forces Institute of Pathology Rawalpindi. Pakistan J Pathol 1993; 4: 107-10.

19. Saeed M, Khawaja K, Rizwana I, Malik I, Rizvi J, Khan A. A clinicopathological analysis of ovarian tumors. J Pak Med Assoc 1991; 41: 161-3.
20. Rashid S, Saman G, Ali A. Clinicopathological study of ovarian cancer. Mother & Child 1998; 36: 117-25.
21. Odukogbe AA, Adebamowo CA, Ola B, Olayemi O, Oladokum A, Adeuole IF et al. Ovarian cancer in Ibadan: Characteristics and Management. J Obstet Gynecol 2004; 24: 294-7.
22. Nieto JJ, Crow J, Sundaresan M, Constatinovici N, Perett CW, Maclean AB et al. Ovarian epithelial dysplasia in relation to ovulation induction and nulliparity. Gynecol Oncol 2001; 82: 344-9.