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ANALYSIS OF SYMPTOMS IN OVARIAN CANCER AND ITS HISTOPATHOLOGICAL CORRELATION: A CROSS SECTIONAL STUDY

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ABSTRACT Ovarian cancer is the fifth common cancer affecting the population and it is a silent killer, as it is diagnosed in later stages. The symptoms of ovarian cancer are nonspecific and a screening tool for ovarian cancer is not there. Diagnosis of ovarian cancer is often delayed due to their presentation with vague and nonspecific symptoms. This study tried to evaluate the symptoms in patients with ovarian cancer and correlate them with the type and stage of malignancy. **Objective:** Analyze the type, duration and frequency of the symptoms in patients with ovarian cancer and to correlate these symptoms with the type of malignancy and stage of the disease. **Methods:** All patients admitted to the Gynaecology Department of Government Medical College, Thrissur with suspected ovarian cancer during the study period were recruited and surveyed using a baseline health questionnaire and a symptom index assessment form suggested by Goff et al was used (1). Assessment was then done to look for any correlation between the symptom duration, severity and frequency of symptoms and the type of ovarian malignancy. **Results and Discussion-** Fatigue followed by indigestion, increase in abdominal size, abdominal bloating, backache, feeling full quickly were the most common symptoms. A mean of 7.6 symptoms out of 23 symptoms enquired about in these women were present for a duration of 1 - 4 months. Abdominal bloating sensation was significantly increased in patients more than 50yrs of age. A rise in CA125 value was also associated significantly with fatigue and abdominal bloating sensation. Epithelial ovarian tumors were found to be significantly associated with indigestion and feeling of fullness quickly. Non epithelial varieties were more often associated with menstrual irregularities and constipation. **Conclusion-** The symptom index can be used as a screening tool for ovarian cancer. Ignoring early warning symptoms will result in late diagnosis of ovarian malignancy and thereby worsen the prognosis for such women.

INTRODUCTION

Ovarian cancer is the fifth most common cancer in the developed countries. It accounts for 4% of all cancers and 31% of gynaecologic cancers. Ovarian cancer is a silent killer due to paucity of symptoms in early stages and due to deep seated and inaccessible location of ovaries. A woman's risk at birth of having ovarian cancer sometime in her life is 1% to 1.5%, and that of dying from ovarian cancer almost 0.5% (2).

The most important reason for a high fatality rate in ovarian cancer is due to delayed diagnosis (1). Over 80% of those with early stage disease have an excellent chance of cure. The most common symptoms were abdominal or gastrointestinal, whereas gynaecologic symptoms were the least common (1). Women with ovarian cancer had abdominal, pelvic, and urinary symptoms that were significantly more frequent, more severe, and of shorter duration than the symptoms reported by women who visited primary care clinics (1). In some patients, symptoms may facilitate earlier detection. Symptoms such as bloating, increased abdominal size, feeling of fullness quickly after taking food, urinary symptoms, and pelvic and abdominal pain were identified significantly more frequently among women with ovarian cancer than among women in the clinic population (2). Symptom triggered screening is feasible and acceptable in a primary care clinic.

METHODOLOGY

Study Design

This is a cross sectional study to analyze the symptoms of ovarian cancer and correlate them with the histopathological diagnosis and stage of the disease.

Study Setting

The study was carried out in Government Medical College, Thrissur. This hospital is a tertiary care referral center for Thrissur and Palakkad districts. All patients with suspected ovarian tumor attending the Gynecology OPD and Gynecology casualty during the period of the study were admitted and evaluated. All patients undergoing surgery (staging laparotomy with optimal or suboptimal debulking, interval cytoreduction, biopsy, FNAC) were followed up and their histopathological reports and subsequent therapy evaluated and recorded through a study period of 12 months.

Study Population

The study population included all women admitted to Department of Obstetrics and Gynaecology with ovarian cancer during the study period.

Inclusion criteria

- Patients admitted with primary ovarian cancers
- Patients who underwent staging laparotomy/ FNAC/ ascitic tap/ neoadjuvant chemotherapy / interval cytoreduction for ovarian mass.
- Patients who were willing to participate in the study and for follow up

Exclusion criteria

- Patients with secondary ovarian malignancy
- Those with hereditary ovarian cancers

Method Of Study:

All patients who got admitted to the Gynaecology Department of Government Medical College, Thrissur with suspected ovarian cancer during the study period were counselled and a signed consent was obtained for being part of the study. They were surveyed on the basis of a baseline health questionnaire, with demographic and health history information and a symptom index assessment form were filled up. Questionnaire format was taken from the study of Goff et al (1). The interview was conducted by a single researcher. A woman was considered positive for the index if she reports at least one index symptom that started within the period of interest. All the responses to the questions were on a 5point scale. Symptom index was considered positive if any one of the symptoms bloating sensation, increased abdominal size, pelvic and abdominal pain, difficulty in eating, feeling full quickly ☐ if the symptoms occurred for >12 days a month and if present of < 1year. After this symptom analysis in patients, they were followed up during and after surgery with histopathology report. Correlation between the symptom duration, severity and frequency with particular type of ovarian malignancy was assessed.

RESULTS

The study was done in 82 patients who presented with symptoms suggestive of ovarian cancer and were diagnosed to have ovarian cancer during the study period of 1 year. There were 167 cases of gynecological malignancy diagnosed and treated during the study period. Majority, 101 patients had malignant ovarian tumor, 54 had carcinoma endometrium, 9 had carcinoma cervix, 1 each of malignant melanoma, carcinoma vulva and choriocarcinoma. Out of 101 cases of ovarian tumor, 82 subjects were enrolled in the study. 19 women were not included in the study. They included 2 with Krukenberg☐s tumor, 4 with a family history of other gastrointestinal and breast cancer, 4 women not willing to participate in the study and 9 patients

whose histopathology report turned out as borderline ovarian tumor. Among the symptoms, most common symptoms reported were fatigue followed by indigestion, increase in abdominal size, abdominal bloating, backache, feeling full quickly, weight loss, pelvic pain, abdominal pain, feeling of abdominal mass. Other symptoms were less prevalent.

In the study group 41.5% experienced mild symptoms, 35.4% had moderate symptoms and only 1.2% did not have any symptom and were diagnosed to have ovarian malignancy during routine checkup.

In the present study majority of patients (29.2%) 24/82 had symptoms 7 -12 days per month, 20 patients had symptoms for 13- 19 days per month, 19 had symptoms only for 3 ☐ 6 days and 10 had symptoms on almost all the days. Most of the patients ,51, in the present study had symptoms for a period of 1 ☐ 4 months, 20 patients had symptoms for less than 1month and 11 patients had symptoms for more than 5 months.

Table. 1. Percentage distribution of the sample according to number of symptoms

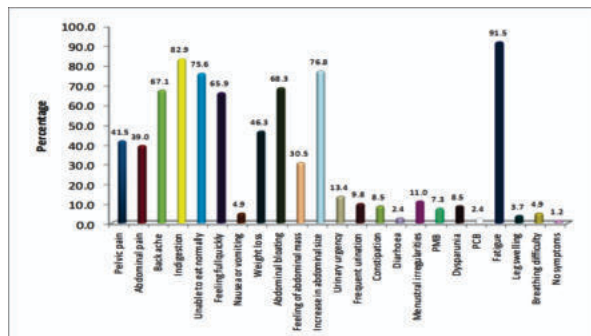| Number of symptoms	Count	Percent
1 - 3	4	4.9
4 - 6	19	23.2
7 - 9	42	51.2
10 - 12	17	20.7
Mean ± SD	7.6 ± 2.3	

Fig.1 Percentage distribution of the sample according to symptoms of ovarian cancer

According to this study 51.2% of the subjects experienced 7 -9 symptoms, 23.2% had 4-6 symptoms and 20.7% had 10-12 symptoms. A mean of 7.6 symptoms were present in the patients with ovarian cancer in this study.

The most common symptom complex associated was abdominal pain, abdominal bloating sensation, fatigue and increase in abdominal size. This symptom complex was found in 37.8% cases in the present study.

There was no significant association between the prevalence of symptoms among different stages of ovarian cancer in this study. The study also identified a high odds ratio between the benign and malignant groups for difficulty eating

The symptoms like indigestion (p value = 0.04) and unable to eat normally (p value = 0.016) was significantly associated with serous cystadenocarcinoma, whereas menstrual irregularities (p value = 0.00) and constipation (p value = 0.007) were significantly associated with other rare varieties of cancers like dysgerminoma, endometroid adenocarcinoma and mixed germ cell tumour.

The study found the association of 23 symptoms with ovarian cancer which can be present in early stages. Detection of these symptoms and its evaluation helps to diagnose ovarian cancer in early stages.

Ovarian cancer is more prevalent in age group >50yrs, mainly postmenopausal, multiparous women, belonging to the lower socioeconomic group with no history of intake of oral contraceptives.

Fatigue, increase in abdominal size, abdominal bloating and backache were the common symptoms associated with the patients. They experienced mild to moderate symptoms for a period of 1-4 months with 7- 12 days frequency in a month. Abdominal bloating and weight

loss had significant association with malignancy in patients >50yrs. CA 125 value more than 35 is significantly associated with symptoms of fatigue, abdominal bloating, indigestion and menstrual irregularities. Indigestion and feeling of fullness quickly are symptoms significantly associated with serous cystadenocarcinoma. Menstrual irregularities and constipation were significantly associated with other uncommon varieties of ovarian cancer.

DISCUSSION

The study was done in 82 patients who presented with symptoms suggestive of ovarian cancer and were diagnosed to have ovarian cancer during the study period of 1 year. Their symptoms were evaluated by using a questionnaire suggested by Goff et al (1). This study showed that most women had symptoms which could be attributed to the ovarian malignancy. 41.5% of the women with ovarian cancer experienced mild symptoms, 35.4% had moderate symptoms while only 1.2% had no symptoms. The mean age of patients who participated in the study was 59.2 ± 12.4, ie; they were mostly in the postmenopausal age group. The incidence of ovarian cancer has been shown to decrease with increasing parity (2). But this study found that ovarian cancer was associated with increasing parity. This difference may be because of decrease in number of patients who are nulliparous in our setup. A study done by Melin et al (3) showed that parity has no effect in the development of cancer. Early age of menarche was found to have no association with the development of ovarian cancer in this study, similar to the meta analysis of epidemiological studies by Ting Ting Gong et al. (4).

Epidemiologically ovarian cancer incidence was found to be higher in patients who have never married than in married women. In this study, majority of patients were married (94.5%). But the US Third National Cancer Survey, 1969-71, found that the incidence of ovarian cancer is higher in women who had never married than in those who had.

This study found only 4 women with ovarian cancer had history of usage of Oral Contraceptive Pills while the rest ,72, had not taken OCP☐s in their life time. Studies showed that the usage of oral contraceptive pills reduce the incidence of ovarian cancer. The risk of developing invasive cancer decreased by about 16% for those who reported ever taking oral contraceptives and for every five years patients continued to use OCP☐s, the risk decreased by 13% (5).

Majority of the women, 78 out of 82, did not have a history of infertility. Most of them were fertile women. But earlier studies have shown that infertile women are at higher risk than fertile women, because of the use of fertility drugs like ovarian follicle stimulating drugs (2).

The study subjects had different comorbidities, which included diabetes mellitus, hypertension and dyslipidemia. 32 (39%) of the patients did not have any comorbidity while the rest had a single or a combination of comorbidities. Metabolic syndrome and its components were associated with majority of cases of ovarian cancer in this study. A study done by Ying Chen et al. (6) showed that epithelial ovarian cancer was significantly associated with metabolic syndrome in cases compared to controls. Most of the patients ,68, were with normal BMI, 8 were obese and 6 were underweight. The malnourished patients had advanced stages of the disease. 35(42.6%) of women with ovarian malignancy were diagnosed at stage 2, 29 (35.4%) were diagnosed at stage 3, 11(13.4%) were diagnosed at stage 1 and 7 were diagnosed in advanced stage 4. Therefore a large majority of the patients were diagnosed at stages 2 and 3.

Survival rates for women with earlystage ovarian carcinoma range from 70% to 90% compared with 20☐30% for women with advanced disease. Hence an attempt to increase awareness about symptoms of ovarian malignancy among healthcare providers and the general population is essential for diagnosis in the early stages to improve outcomes. This study emphasizes the fact that most women with ovarian malignancy do have symptoms which are often overlooked or not considered as serious until well advanced in the stage of the disease. Use of a well defined symptom index to evaluate cases of ovarian malignancy and to correlate with the type of tumour are strengths of the study.

The limitations of the study are because of the small sample size and short duration of the study which was only for a year. The follow up of these women following treatment is needed to correlate morbidity,

prognosis and survival.

CONCLUSION
This study concluded that a symptom index like Goff index can be used as a screening tool for ovarian cancer. It is important to increase the awareness about the nonspecific symptoms in ovarian cancer for early detection and treatment. Women are often unaware of what constitutes normal physiologic changes with aging as opposed to pathologic changes. Educational efforts need to focus on this issue.

In this study a patient with ovarian cancer had the symptoms mainly abdominal pain, abdominal bloating sensation, fatigue and feeling of fullness quickly for a mean period of 7-9 days per month for a duration of 1-4 months in mild to moderate severity. Hence symptom index can be used as a screening tool for ovarian cancer which is very cheap, economical and feasible in low resource settings. Increased awareness of its symptoms and early detection will definitely improve the prognosis and outcome of women with ovarian malignancy.

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Ethical approval: The study was approved by institutional ethics committee.

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