ABSTRACT

Introduction: Ovarian cancer accounts for four percent of all cancer in women worldwide. It is considered as the silent killer, because symptoms do not develop until the disease reached advanced stages. Majority of women are diagnosed at advanced stages when prognosis is poor. This study was carried out with an aim to find out association of Symptom Index with ovarian cancer.

Methods: A hospital based case control study was conducted over one year in department of Obstetrics and Gynecology, TUTH, Kathmandu. All patients visiting to Gynecology OPD or admitted to Female Surgery Ward with histopathology confirmed ovarian cancer were included. Age matched women with benign ovarian tumor at the ratio of 1:2 were taken as controls. All women were inquired regarding the occurrence of eight symptoms associated with ovarian cancer. A symptom index was considered positive if any of those symptoms occurred >12 times per month but were present for <1 year.

Results: There were 30 cases and 60 controls. Twenty-nine (96.7%) cases and 56 (93.4%) controls presented with abdominal pain but it was not statistically significant. However, abdominal bloating in 56.7% vs 8.3% [OR-14.4 (4.5-46.2)], increased abdominal size in 40% vs 11.6% [OR- 5.04 (1.7-14.8)], difficulty in eating in 30% vs 17% [OR- 25.3 (3.02-211.7)], and feeling full in 23.3% of vs 1.7% [OR-17.9 (2.09-154.1)], all were statistically significant.

Conclusions: Symptoms are present in a significant number of women with ovarian cancer. So, evaluating women with specific symptoms of recent onset helps to make the early diagnosis of ovarian cancer.

Keywords: ovarian cancer; pelvic pain; symptom index.

INTRODUCTION

Cancer is among the leading causes of death worldwide, accounting for 8.8 million deaths in 2015.¹ Ovarian cancer accounts for four percent of all cancer in women with more than 200000 new cases each year and 6.6 new cases per 100,000 women per year;² It is seventh most common causes of death from cancer in Asia.³ The incidence of ovarian cancer in Nepal is also increasing with incidence of 0.8% in 2003 and 2.3% in 2013.⁴ World Health Organization (WHO) has estimated that the ovarian cancer is responsible for 7% of total deaths from cancer among women in Nepal.⁵

In early cancer (FIGO stage 1 and 2), the survival is 80-90% compared to 25% in late cancers (FIGO 3 and 4) and is associated with good prognosis.⁶-⁷ Ovarian cancer was said to be the silent killer as symptoms did not develop until the disease reached advanced stages, when the chance of a cure was poor.⁸ Studies of symptoms have confirmed that women with ovarian cancer have gastrointestinal, abdominal, and urinary symptoms.⁹-¹¹

This study was carried out with an aim to find out association of Symptom Index (SI) with ovarian cancer.

METHODS

It was a hospital based case control study conducted in department of Gynecology and
Obstetrics, TUTH, Maharajganj, Kathmandu from 13th April 2013 to 12th April 2014.

All patient visiting Gynecology Outpatient Department (OPD) or admitted in the Female Surgical Ward (FSW) with histopathology confirmed ovarian cancer were included. Controls were taken as age matched women with benign ovarian tumor at the ratio of 1:2. The cases included women with ovarian tumor/ adnexal mass, who underwent laparotomy and later confirmed as ovarian cancer histologically, women admitted in the FSW with histopathological /FNAC diagnosis of ovarian tumor for neoadjuvant or adjuvant chemotherapy, patients of ovarian malignancy coming for follow up after surgery either to OPD or to FSW. Similarly, those cases admitted to female surgical ward with suspicion of malignancy and who underwent laparotomy for the same were also included, but taken into study for analysis only if histopathological diagnosis was confirmed. Controls included women admitted to FSW for adnexal masses other than suspected or proven malignancy by examination or ultrasonography and histopathology as well cases suspected as malignancy who underwent surgery but histopathological findings of benign lesion.

Women in whom the primary diagnosis of malignancy was in doubt or with malignancy of other organs were excluded. Patients who could not recall their symptoms presenting before treatment/diagnosis were also excluded from the study.

All patients were explained about the study and consent was taken. Those who agreed to participate were taken in the study. The age, parity, education status and ethnicity of both cases and controls were taken into account. The histopathology diagnosis of all women was noted. Among cases the surgical stage of the tumor was noted from the operation note as well as from the discharge paper or referral documents whatever is available with the patient. Patients were asked in details regarding the symptoms associated with ovarian cancer. All information was taken and a pre-fixed questionnaire filled up.

The symptom included: Pelvic pain, Abdominal pain, Increased bloating, Abdominal bloating, Feeling full, Difficulty eating, Urinary urgency, Urinary frequency.

A symptom index was considered positive if any of those symptoms occurred >12 times per month but were present for <1 year.

Information collected was coded and daily entry was done into master chart. The data analysis was done using Microsoft Excel 2013 and SPSS 19 software. To determine the statistical symptom index, chi square test was used. Odds Ratio (OR) for each symptom index was calculated. P value was taken as significant if < 0.05.

RESULTS

Total of 48 women with suspected ovarian cancer were enrolled, out of which 30 women had histopathology reports confirming ovarian cancer and 18 patients were excluded from the study as they had negative histopathology (HPE) reports for ovarian malignancy. Age matched 60 women with benign ovarian tumors were taken as controls. The baseline characteristics of the cases and controls are shown (Table 1). There was no significant difference in baseline characteristics between cases and controls. Twenty four (80%) cases at the time of presentation were in early stage of ovarian cancer and 6 (20%) in late stage of disease. Early stages included stage I and stage II diseases and late stages included stage III and stage IV diseases. Histopathology of the cases and controls are presented (Table 2).

Presence of various symptoms included in Symptom Index (SI) in both cases and controls is presented in Table 3. Around 96% of cases and 93% controls presented with abdominal pain but it was not statistically significant. However, abdominal bloating, increased abdominal size, difficulty eating and feeling of fullness were significantly higher in cases compared to controls. Urinary symptoms, as urinary urgency and urinary frequency were neither found in cases nor in controls.

Table 1. Baseline Characteristics of Cases and Controls.

| Characteristics | Cases n=30(%) | Controls n=60 (%) | P |
|----------------|--------------|------------------|---|
| Mean Age (Years) | 45.67±9.91 | 43.68±9.28 | 0.353 |
| Mean Parity | 2.6±0.85 | 2.35±0.95 | 0.229 |
Table 2. Histopathology of the participants.

| Cases (n=30)          | Controls (n=60)          | Histopathology | Histopathology |
|-----------------------|--------------------------|----------------|----------------|
| Serous cyst adenocarcinoma | Mature cystic teratoma | 12 (40)        | 18 (30)        |
| Mucinous cyst adenocarcinoma | Endometriotic Cyst     | 6 (20)         | 18 (30)        |
| Endometroid ovarian cancer | Serous Cystadenoma    | 2 (6.67)       | 13 (21.67)     |
| Clear cell carcinoma    | Mucinous Cystadenoma    | 1 (3.33)       | 11 (18.33)     |
| Granulosa cell tumor    |                          | 3 (10)         |                |
| Squamous cell carcinoma arising from the mature teratoma |                          | 2 (6.67)       |                |
| Germ cell tumor         |                          | 2 (6.67)       |                |
| Poorly differentiated ovarian cancer |                          | 1 (3.33)       |                |
| Metastatic adenocarcinoma |                          | 1 (3.33)       |                |

Table 3. Symptom Index in Cases And Controls.

| Symptoms                  | Cases n=30 (%) | Controls n=60(%) | OR (CI=95%) | P     |
|---------------------------|----------------|------------------|-------------|-------|
| Abdominal Pain            | 29 (96.7)      | 56 (93.4)        | 2.07 (0.221-19.4) | 0.515 |
| Pelvic Pain               | 2 (6.7)        | 6 (10)           | 0.64 (0.12-3.4)   | 0.600 |
| Abdominal Bloating        | 17 (56.7)      | 5 (8.3)          | 14.4 (4.5-46.2)   | 0.001 |
| Increased Abdominal       | 12 (40)        | 7 (11.6)         | 5.04 (1.7-14.8)   | 0.002 |
| Difficulty Eating         | 9 (30)         | 1 (1.7)          | 25.3 (3.02-211.7) | 0.001 |
| Feeling Full              | 7 (23.3)       | 1 (1.7)          | 17.9 (2.09-154.1) | 0.001 |

DISCUSSION

Early detection of ovarian cancer significantly improves the survival of patients with ovarian cancer. Early recognition of symptoms by both medical providers and patients is crucial in order to improve the outcomes of the patients. In our study we focused on role of symptom recognition in the early diagnosis of ovarian cancer.

Increasing age is a major risk factor, and the highest incidence rates are for women aged 60-64 and above. In our study 30 (50%) of cases were in the age group of 40-50 years. Mean age of cases was 45.67 years with the smallest age group being 20-30 years and largest age group being more than 60 years.

Our study showed that epithelial ovarian cancers were more than 50% of histopathology proven ovarian cancer. In the similar study done by Kaku T, et al showed that epithelial ovarian tumors are the majority of malignant ovarian tumors with histological types of serous, mucinous, endometrioid, clear cell, mixed epithelial tumor, undifferentiated carcinoma, and others.

The most commonly reported symptoms were abdominal pain, increased abdominal size, abdominal bloating, difficulty eating and feeling full in this study. All cases did not have urinary frequency and urinary urgency. Data in this study showed that 96% cases were with abdominal pain 7% with pelvic pain. However, abdominal bloating were found in 17 (56.7%) cases with OR 14.4(14.5-46.2), increased abdominal size in 12 (40%) cases with OR 5.04(1.7-14.8), difficulty in eating 9 (30%) cases with OR 25.3(3.02-211.7) and feeling full 7(23.3%) cases with OR 17.9(2.09-154.1). Similarly, Bankhead C R and colleagues in a meta-analysis found that the most common symptoms were abdominal pain; abdominal bloating and abdominal swelling and most of them experienced these symptoms for 1-6 months. Similar to this study, Goff et al in their study reported that found that increased abdominal size was the most common symptom (61%) followed by abdominal bloating (57%). Unlike this study,
Kirwan et al and Olsen et al found abdominal pain was only reported symptom though abdominal pain was only one of the symptoms in this study.\textsuperscript{15,16} Paulsen et al reported that abdominal distension was the second most common symptom, with 44\% of women with invasive tumours.\textsuperscript{17}

None of the cases in our study had urinary problems as urgency, frequency. However, various studies have also reported that urinary frequency and urgency were commonly reported symptoms.\textsuperscript{10,16,18} Fitch et al found abdominal pain in 77\%, urinary symptoms in 34\%, and pelvic pain in 26\% women with ovarian cancer.\textsuperscript{19} These studies had cases more in advanced stages where urinary symptom is usually involved. Webb et al urinary symptoms were experienced in late stage of disease (stage III and IV).\textsuperscript{20} But, cases in the study were mainly in early stage. The other probable reasons could be less sample size and short duration of study. Pelvic pain was found in 6.7\% cases in this study being not statistically significant but study done by Hartman et al found symptom of pelvic pain in 60\% of women with malignant tumors.\textsuperscript{21}

CONCLUSIONS

Our study found that most women presented in early stage because of presence of gastrointestinal symptoms. In this study twenty-nine (96.7\%) cases had abdominal pain. And most of them were in early stage. Similarly, Vine et al found that abdominal pain was the most commonly reported symptom for early and advanced stages.\textsuperscript{22} Similar results were found in the study by Webb et al. where, abdominal pain and abdominal swelling were most commonly reported as the first symptoms in early as well as late disease.\textsuperscript{20} Similar to this study, Eltabbakh et al in their study found that 78\% of the patients in early stage had presenting symptom of abdominal pain. In the same study pelvic pain was found in 34.7\%, abdominal bloating in 31.9\%.\textsuperscript{23} However various studies have reported that advanced stage ovarian cancer had a higher number of symptoms.\textsuperscript{24,25} This may be due to recall bias as patients were interviewed during various stages of treatment as later after or during treatment and follow up. The other reason could be small number of patients in late stage disease (17\%) and duration of the study was short comparing with longer duration of study in other studies.

CONFLICT OF INTEREST: None.

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