Original Article

Risk factors and symptoms of ovarian cancer: Is the GP aware?

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Abstract

Introduction: Epithelial ovarian cancers are the leading cause of death amongst all gynecological cancers. Mostly ovarian cancer remains asymptomatic till it becomes huge in size. Catching it early is challenging as no screening test is available. Goff symptom index (GSI) is a symptom-based tool available for primary health care settings for early detection of ovarian cancer. This study was carried out to assess knowledge, perception and understanding of general practitioners practicing in and around Pune about symptoms and risk factors of ovarian cancer. **Material and Methods:** Cross sectional study using online Google forms. The Google form was created based on a pre-validated Oxford University OvCAM tool. It included the Goff Symptoms index-based questions. Questions were open, as well as, closed ended type. We received 150 responses. **Results:** Respondent practitioners were able to identify three common symptoms as abdominal distention, pain, and menstrual irregularity. Family history of ovarian and breast cancer as a risk factor was missed by 49% and 70% responded abdominal ultrasound as first investigation. Clinical pelvic examination was not quoted by any of the participants. Majority of them were aware that Pap smear has no role for screening ovarian cancer. **Conclusion:** The general practitioners around Pune are aware about persistent pain and abdominal swelling as possible symptoms of ovarian cancer. Continuous medical education regarding risk factors of ovarian cancer, exposure to tools like Goff symptom index will be helpful in developing awareness other nonspecific symptoms and timely referral of patients for further evaluation.

Keywords: ovarian cancer, Goff symptom index, general practitioner, survey

Introduction

According to Globocan 2018, around 2,94,714 new cases of cancer ovary are diagnosed every year causing deaths in 1,84,800 cases worldwide. Risk of developing ovarian cancer in Indian women before the age of 75, is 4.6%. The top five common female cancers seen in India are: breast, cervix uteri, ovary, lip and oral cavity, colorectal[(1)]. According to cell of origin, there are three broad categories of malignant ovarian tumors: epithelial ovarian cancers, germ cell tumors and sex chord stromal tumors. Epithelial ovarian cancers constitute 90% of all ovarian malignancies[(2)]. Epithelial ovarian cancers are the leading cause of death amongst all gynecological cancers. It presents with following epidemiology and risk factors - Age: 50% of ovarian cancers are seen above 65 years of age[(2)], genetic factors: 18 to 24% of invasive epithelial cancers have an autosomal dominant germ line mutation. BRCA1/2 is the most common identified genetic mutation, followed by hereditary nonpolyposis colon cancer (Lynch syndrome), showing MLH1, MSH2, MSH6, PMS2 mutations[(2)]. These patients have strong family history of breast and ovarian cancer. Hormonal and reproductive factors**:** Early menarche, late menopause, endometriosis, nulliparity increase the chance of ovarian cancer[(2)]. High parity, breast feeding, and oral contraceptive (OC) pill use are protective against ovarian cancer[(8)]. Common mechanism involved in these reproductive factors is increase or decrease in number of ovulations that a woman experiences in her lifetime. Suppression of ovulation prevents injury to surface epithelial cells of the ovary. Procedures like tubal ligation and hysterectomy are protective against ovarian cancer[(2)]. Pelvic inflammatory disease (PID) and endometriosis are found to be associated with ovarian cancer[(2)]. The intensive release of cytokines and

inflammatory infiltrates are responsible for increased risk of cancer in these patients. Lifestyle factors like diet, smoking, physical exercise have not directly implicated in ovarian carcinogenesis[2]. But long-term interventions like low fat high vegetarian diet, cessation of smoking has shown beneficial effect on carcinogenesis as well as survival rates[2].

Clinical presentation

Variable clinical presentation is seen depending upon the size of the tumor. Most of the time ovarian cancer remains asymptomatic till it becomes very large in size. Once it is large enough to compress the surrounding structures, it presents with pressure symptoms like:

- Chronic pelvic pain, backache
- Urinary symptoms like urgency, dysuria, and frequency
- Constipation due to recto sigmoid pressure
- Acute abdomen due to complications in tumor like torsion, rupture, hemorrhage
- Non-specific symptoms like anorexia, fatigue, early satiety is common in advanced malignant tumors
- Bloating, diffuse abdominal pain due to peritoneal infiltration
- Abdominal distention, dyspnea, and electrolyte imbalance due to large volume ascites
- DVT and hyper coagulopathy

As the symptoms often develop late, ovarian cancer is called as 'silent killer'[3]. Worldwide incidence of ovarian cancer is 2.5%, but it is responsible for 5% deaths due to late diagnosis. If ovarian cancer is diagnosed while the disease is localized to ovary, the overall five year survival is 70-90%[3]. Catching up them at this stage is challenging as the patient suffers from very vague non-specific symptoms like back pain, abdominal bloating, indigestion, altered bowel habits etc. Most of these symptoms make the patient consult to their primary care physicians.

Currently, there is no effective screening available. High index of suspicion is the key to early diagnosis[4]. UKCTOCS (United Kingdom collaborative trial of ovarian cancer screening) based on transvaginal ultrasound and tumor marker CA 125, proved that this approach is neither useful nor cost effective as mass screening method[5]. Attempts are being made to make algorithms based on symptoms suggestive of ovarian cancer. Various tools based on symptom index are available in primary health care setting. These can be used to pick up cases for further work up for ovarian cancer. GSI consisting six symptoms pelvic pain, abdominal pain, increased abdominal size, bloating, difficulty in eating and a feeling of fullness was proposed by Goff et al in 2007[3]. Modifications were suggested in GSI by adding symptoms such as urinary urgency/frequency, loss of appetite and loss of weight[6,7]. The symptomatic assessment of all women at every visit is an integral part of history taking in advanced countries like UK[8]. It is observed that when there are persistent symptoms occurring more than 12 times a month over 12 months, likelihood of early stage ovarian cancer is high[3,6].

This study was carried out to assess knowledge, perception and practice of general practitioners practicing in and around Pune about symptoms and risk factors of ovarian cancer.

Material and Methods

This cross-sectional study was performed based on online survey using Google forms amongst general practitioners practicing in and around Pune from February 2019 to July 2019. There was purposive sampling as all consenting general practitioners in mailing list available through local directory and hospital register were selected for the survey. Total 200 general practitioners were contacted, out of which 150 responses were analyzed. The list of general practitioners practicing in and around Pune was collected from different databases. Their e-mail addresses and mobile numbers were recorded. A link of survey was sent to the respective e-mail addresses. They were given acknowledgement after submission. Up to three reminders were sent to fill the survey form for maximum participation. The Google form was created based on a pre-validated Oxford University ovarian cancer awareness measure tool (Ovary CAM)[8]. It was conducted as anonymous response. There were seven open ended questions addressing the knowledge, perception and understanding about symptomatology and clinical presentation of ovarian cancer. In the first part, the survey contained five points related to demography of the responder. In the second part, there were open ended questions like 'there are several warning signs and symptoms of ovarian cancer. Please name as many as you can think of'. The next part of

survey was not accessible unless first question was answered. In third part there were closed ended questions like 'the following may or may not be the warning signs of ovarian cancer, we are interested in your opinion.' Options provided were persistent pain in abdomen, persistent pain in pelvis, persistent bloating, abdominal distension, persistent feeling of fullness of stomach, increased frequency of micturition, altered bowel habits. In the fourth part, there were questions addressing understanding and perception about risk factors of ovarian cancer. Participants were asked to answer on five-point Likert scale as strongly agree/agree/not sure/disagree/strongly disagree e.g., 'these are some things that can increase a woman's chance of developing ovarian cancer. How much do you agree that each of these can increase the chance of developing ovarian cancer?' -Having a close relative with ovarian cancer, having a past history of breast cancer, being overweight (BMI over 25), having endometriosis, having ovarian cysts. In the fifth part, participant's perception about the condition, like 'how confident he/she felt about detecting ovarian cancer symptoms at early stage on five-point Likert scale?' It generally took around 15-20 minutes to fill the questionnaire.

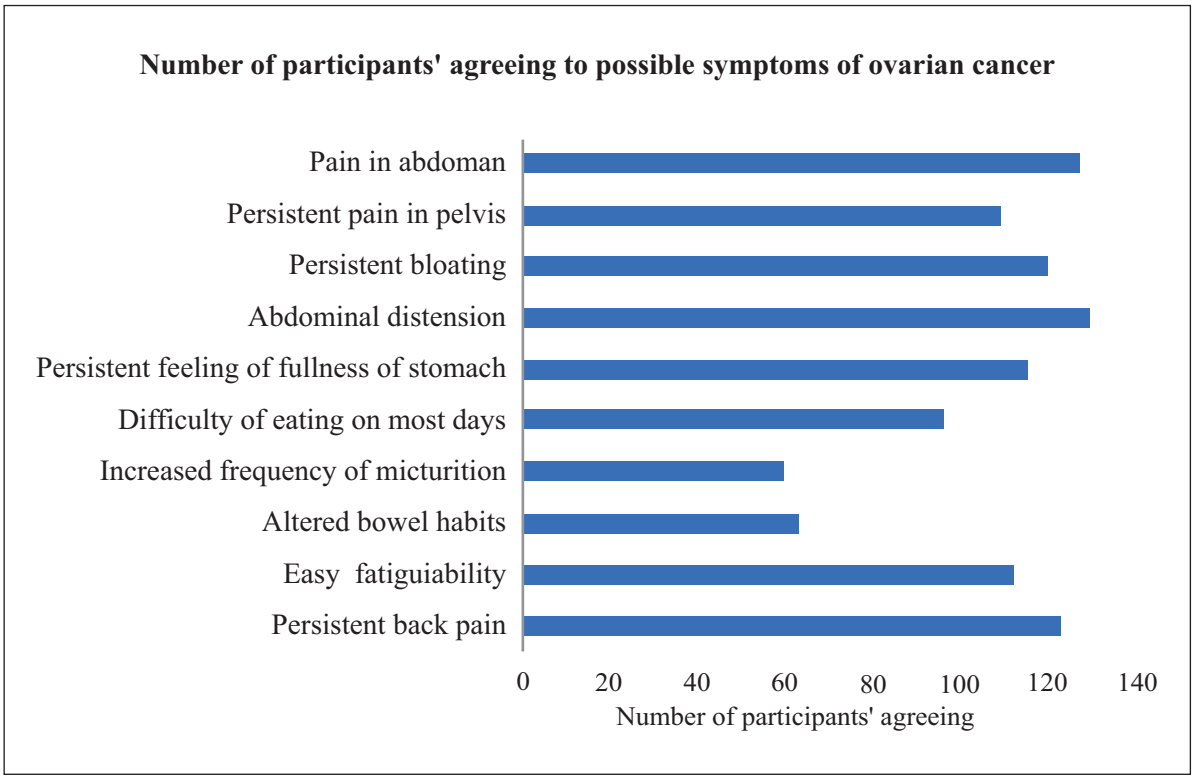
Results

Out of 200 contacts, 167 participants responded to the survey (83.5%). Out of these 167 responses, 17 forms were found incompletely filled hence total 150 responses were considered for analysis. Out of 150 participants, 80 were female (53.33%) and 70 were male (46.66%). Practitioners having less than 15 years of practice were 54% of the total whereas 46% were in general practice for more than 15 years. Only 6 out of 150 practitioners were practicing in both urban and rural areas; rests all were working in urban area. Total 71 practitioners (47.33%) were attending to less than 10 female patients per day while 79 practitioners (52.66%) were attending more than 10 female patients per day. As shown in table 1, most identified symptom of ovarian cancer was abdominal swelling, 74% responders quoted the same.

Table 1: Participant's response about most common symptom associated with ovarian cancer (n=150)

Most named symptom of Ovarian cancer	Participants n (%)
Pain	59 (39.3)
Abdominal swelling, abdominal distension, lump in abdomen	112 (74.6)
Weight loss	21 (14)
Menstrual irregularity	51 (34)
Bloating	16 (10.6)
No complaints	8 (5.3)
Nausea	2 (1.3)

When asked whether following may be the symptoms of cancer ovary, the responses were as shown in graph 1:



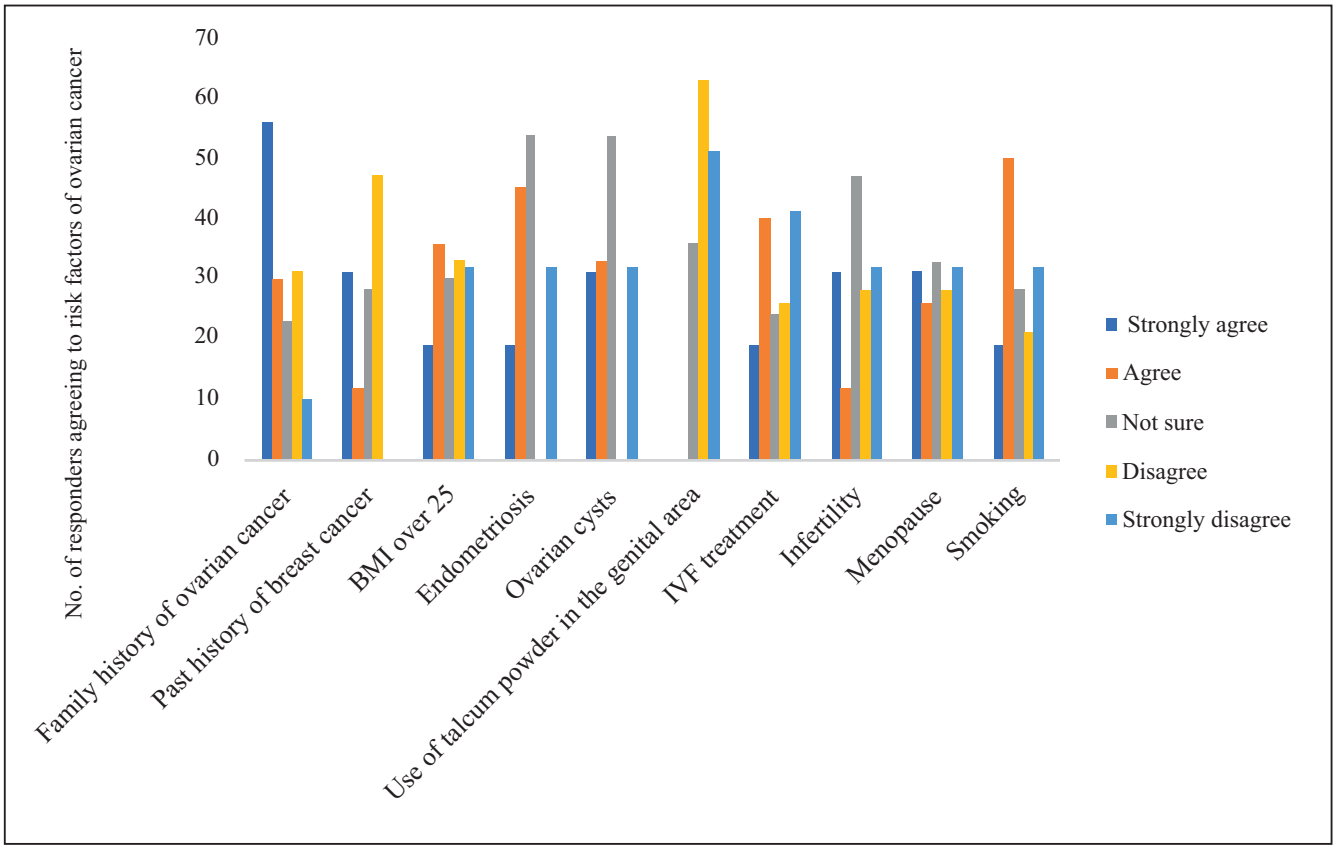
Graph 1: Number of participants agreeing to symptom complex suggestive of ovarian cancer after giving a cue (list of symptoms)

About investigations/risk factors in a case of suspected ovarian cancer, the responses were as shown in table 2:

Table 2: General practitioners' knowledge about risk factors and investigations in cases of ovarian cancer (n=150)

Suggested investigation	**No. of responders n (%)**
USG abdomen Pelvis/TVS	138 (92)
USG with CA 125	27 (18)
Excisional biopsy	12 (8)
USG with CEA	12 (8)
USG with Hemogram	24 (16)
In next one year who is likely to develop ovarian cancer?	
Ovarian cancer is unrelated to age	77 (51.3)
70 years old women	33 (22)
50 years old	28 (18.6)
30 years old	12 (8)
What are the risk factors for developing ovarian cancer?	
Family history	50 (33.3)
Nulliparity/infertility	44 (29.3)
OC Pills	16 (10.6)
Age	29 (19.3)
Menopause	13 (8.6)
History of molar pregnancy	12 (8)
History of Ca breast	27 (18)

When prompted to think and asked about what will increase the chance of a woman of developing cancer ovary the responses were as shown in graph 2:



Graph 2: Numbers of general practitioners' agreement about enlisted risk factors of ovarian cancer

A correct response that ovarian cancer may happen at any age but commonly after 50 years of age, was given by 138 out of 150 (92%). Family history and personal history of breast cancer as a risk factor were identified by 77 (51%) of practitioners. Remaining 49% of the practitioners were not aware of the importance of family history or personal history of breast cancer with respect to ovarian cancer. Endometriosis as a risk factor was identified by 65 (43%) responders. Ovarian cyst as a risk factor was positively confirmed by 43% of the responders. Nulliparity and infertility treatment as a risk factor was agreed upon by 102(68%) general practitioners. Use of talcum powder in genital area as a risk factor for ovarian malignancy was dismissed by 104(69%) practitioners. Smoking as a risk factor for ovarian cancer was agreed upon by 59(39%) practitioners. When asked whether Pap smear helps in identifying ovarian cancer, 124 out of 150 (82%) disagreed. A total of 92 out of 150(61%) participating general practitioners said that they were not sure about recognizing symptoms of ovarian cancer.

Discussion

Generally, it is considered that patients of early-stage ovarian cancers rarely have any symptoms. A national survey about ovarian cancer diagnosis by Goff et al in USA analyzed 1725 ovarian cancer patients responses about symptomatology and their medical records from their first hospital visit till the time of diagnosis[9]. This study provided evidence that many of those patients actually had symptoms for at least 12 months before the cancer could be diagnosed. These initial symptoms are nonspecific and hence got ignored by patients as well as their primary health care providers. Goff and colleagues developed a symptom index in which six symptoms were considered significant[3]. Symptoms that were associated independently with cancer were pelvic/abdominal pain, increased abdominal size/bloating, and difficulty eating/feeling full. A symptom index was considered positive if any of those 6 symptoms occurred >12 times per month but were present for < 1 year. In the confirmatory sample, the index had a sensitivity of 56.7 for early-stage disease and 79.5% for advanced-stage disease. Specificity was

90% for women age > 50 years and 86.7% for women age < 50 years [3].

The non-specific early symptoms mimic conditions like Irritable bowel syndrome, dyspepsia, and menopause. Generally, patients visit their primary health care providers for these symptoms. Vagueness of clinical presentation poses a challenge for the general practitioners in considering ovarian cancer as probable diagnosis. Failure to perform a pelvic examination leads to diagnostic delays in this situation. There has been an increase in the research interest for screening of ovarian cancer with majority of research being focused on use of biomarkers and pelvic ultrasound with multimodal assessments for early detection of ovarian cancer[5]. Over the last decade or so, research has also been intensified on symptom-based detection of ovarian cancer with the potential advantage of early detection and timely treatment.

A systematic review by Frie et al has estimated that 93% (95% CI: 92% to 94%) of women experienced symptoms before diagnosis of ovarian cancer only 3-4 months prior[10]. In our survey, we got response rate as 75% after persuasion and reminders. The practitioners belonged to different streams of 'pathies' of medical sciences. The respondent practitioners identified two common symptoms in ovarian cancer as abdominal distention and pain, this is consistent with previous study done by Ketan Gajjar et al[6]. Graph 1 depicts responses after giving a cue to early possible symptoms of ovarian cancer as per Goff index. After giving a cue 80% of the general practitioners agreed to abdominal pain, abdominal distension and persistent backache as significant symptoms, this finding is also consistent with previous study[6].

As depicted in first bar diagram the symptoms like difficulty of eating on most days, increased frequency of micturition and altered bowel habits were least commonly identified symptoms by the general practitioners. This finding is consistent with earlier studies. Thus, GPs in the survey appeared to attach less significance to gastrointestinal symptoms, possibly explaining the reason for higher number of ovarian cancers being referred to other specialties initially. The current observation may suggest that to diagnose the ovarian cancer, equal importance should be given to abdominal, gastrointestinal, and constitutional symptoms. In a study by Hamilton and colleagues, symptoms of abdominal distension, urinary frequency, and abdominal pain remained independently associated with a diagnosis of ovarian cancer[11].

In the settings where self-administered questionnaires are used for patient interviews, even patients attach significance to these symptoms in the order of abdominal bloating > pelvic pain > increased abdominal size > feeling full quickly > unable to eat normally[12,13]. When asked about the first step the practitioners would take once they have suspected ovarian cancer, 100% of the practitioners responded with ultrasonography of abdomen as preferred investigation. It is recommended that any woman with symptoms suggestive of ovarian cancer should have a careful pelvic examination and pelvic ultrasonography[6]. These patients are suggested to be screened with USG abdomen/pelvis and CA 125. Though routine screening of ovarian cancer is not found to be effective in large trials[5]. Majority of the responding practitioners were aware of these investigations.

The next part of questionnaire was about assessing the known risk factor for ovarian cancer. According to latest concept of dualistic model of ovarian carcinogenesis, endometriosis is considered as precursor for type 1 ovarian cancers[14]. In our survey, endometriosis and ovarian cysts as a risk factor were identified by less than 50% of practitioners. Nulliparity and infertility treatment as a risk factor was agreed by 68% of general practitioners. Majority of the responders have said that they are not sure about recognizing symptoms of ovarian cancer. This finding is consistent with Ketan Gajjar et al[6].

Cancer cervix is the most common female genital tract malignancy in India. It is evident from our study that general practitioners are aware that Pap smear is not a screening test for ovarian cancer. Because of varied presentation of ovarian cancers and lack of any specific screening test, it is difficult to catch this entity at early stage. A thorough understanding of the spectrum of non-specific symptomatology in ovarian malignancies can help in making an early diagnosis. Introducing symptom-based screening tool like Goff symptom index may help the general practitioners to consider the diagnosis of ovarian cancer and refer the cases in time. The other advantage of using a symptom-based screening tool is to create awareness among public.

Limitations of the study

Sample size of the study was small and limited to one geographic area. We need a multicentric, multi region study with different health sciences stream groups. We did not ask usual patients' age group and experience of number of ovarian cancer cases seen in the lifetime by the practitioner. If the health care provider is not involved in the susceptible age group patients, the awareness of disease entity may not be updated.

Conclusion

In spite of above limitations our study is able to catch the general level of awareness about risk factors, symptoms, and approach to a patient of ovarian cancer among general practitioners. The general practitioners around Pune are aware about persistent pain and abdominal swelling as possible symptoms of ovarian cancer. Continuous medical education regarding risk factors of ovarian cancer, exposure to tools like Goff symptom index will be helpful in developing awareness other nonspecific symptoms and timely referral of patients for further evaluation.

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References

1. The L. GLOBOCAN 2018: counting the toll of cancer. Lancet (London, England). 2018;22:392(10152):985.
2. Momenimovahed Z, Tiznobaik A, Taheri S, & Salehiniya H. Ovarian cancer in the world: epidemiology and risk factors. Int J Womens Health. 2019;11:287–299.
3. Goff BA, Mandel LS, Drescher CW, Urban N, Gough S, Schurman KM et al. Development of an ovarian cancer symptom index: possibilities for earlier detection. Cancer. 2007;15:109(2):221-7.
4. Ore RM, Baldwin L, Woolum D, Elliott E, Wijers C, Chen CY, et al. Symptoms Relevant to Surveillance for Ovarian Cancer. Diagnostics. 2017;7(1):18.
5. Jacobs IJ, Menon U, Ryan A, Gentry-Maharaj A, Burnell M, Kalsi JK, et al. Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. The Lancet. 2016;5:387(10022):945-56.
6. Gajjar K, Ogden G, Mujahid MI, Razvi K. Symptoms and risk factors of ovarian cancer: a survey in primary care. International Scholarly Research Notices. 2012;2012.
7. Shetty J, Priyadarshini P, Pandey D, Manjunath AP. Modified Goff Symptom Index: Simple triage tool for ovarian malignancy. *Sultan Qaboos Univ Med J*. 2015;15(3):e370-5.
8. Available at: https://www. cancerresearchuk .org/health-professional/awareness-and-prevention/the-cancer-awareness-measures-cam accessed on 7 October 2018.
9. Goff BA, Mandel L, Muntz HG, Melancon CH. Ovarian carcinoma diagnosis: results of a national ovarian cancer survey. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2000 Nov 15;89(10):2068-75.
10. Freij M, Al Qadire M, Khadra M, ALBashtawy M, Tuqan W, Al Faqih M et al. Awareness and knowledge of ovarian cancer symptoms and risk factors: A survey of Jordanian women. Clin. Nurs. Res. 2018;27(7):826-40.
11. Lockwood-Rayermann S, Donovan HS, Rambo D, Kuo CW. Women's awareness of ovarian cancer risks and symptoms: analysis of responses to an online survey shows that women ages 40 and older are not well informed. Am. J. Nurs. 2009;1:36-46.
12. Rossing MA, Wicklund KG, Cushing-Haugen KL, Weiss NS. Predictive value of symptoms for early detection of ovarian cancer. J. Natl. Cancer Inst. 2010;24:102(4):222-9.
13. Hamilton W, Peters TJ, Bankhead C, Sharp D. Risk of ovarian cancer in women with symptoms in primary care: population-based case-control study. Bmj. 2009;26:339:b2998.
14. Kurman RJ, Shih IeM. The Dualistic Model of Ovarian Carcinogenesis: Revisited, Revised, and Expanded. Am J Pathol. 2016;186(4):733-47.