

DOI: <https://doi.org/10.32441/kjps.03.01.p5>

## **Gynecological cancer: Evaluating of Most Prevailing Subtypes of the Disease with Highlighting their Management in Kirkuk City**

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### **ABSTRACT**

Background: Gynecological cancers are group of cancers which occur in female reproductive tract. The corner stone in treating and eliminating this cancer depends mainly on early detection and perfect surgical staging of the disease. Objective: This study focuses on assessing the incidence, stage and treatment pattern of those cancers in Kirkuk city. Methods: A total of 100 females with cancer of gentelial tract were collected from Kirkuk Oncology Center in periods between 2016 November to 2018 August. Results: Most common types of gynecological cancer in this study were: uterine cancer 49%, Ovarian cancer 35%, cervix cancer 6%, GTN 8%, and vaginal cancer 2%. While, the peak age incidence were: uterine and vaginal cancer at age 50-59 years (73.5%, 50%) Ovarian cancer at age 40-49 years 42.9%, and cervix cancer at age 60-69 years 50%. Majority of cases operated by gynecological & obstetrician surgeons were about (62%), and nearly all of patients underwent TAH+BSSOO (92%) with only 2% of cases had PLND. A two years follow up shows recurrence rate of 32%, 28.6%, and 100% for each of uterine, ovaries, and cervical cancer consecutively. Conclusion: Gynecological cancer occurs in younger age group with relatively aggressive stage and high recurrence rate in Kirkuk city.

**Keywords:** Gynecological Cancer, PLND, Kirkuk

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## سرطان النساء : تقييم أكثر الأنواع السائدة من المرض مع تسليط الضوء على طرق

### علاجها في مدينة كركوك

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### الملخص

السرطانات النسائية هي مجموعة من السرطانات التي منشأها من الجهاز التناسلي للأنثى. الكن الاساسي في علاج هذا السرطان والقضاء عليه يعتمد بشكل أساسي على الكشف المبكر والتدريج الجراحي المثالي للمرض. **الهدف:** تركيز هذه الدراسة على تقييم حالات الإصابة بالسرطان ونوعها وطرق علاجها في مدينة كركوك. **الطريقة:** تم جمع ما مجموعه 100 من الإناث المصابات بسرطان الجهاز التناسلي من مركز كركوك التخصصي لعلاج الأورام في فترة ما بين نوفمبر 2016 إلى أغسطس 2018. **النتائج:** أكثر أنواع سرطان النساء شيوعاً في هذه الدراسة هي: سرطان الرحم 49% ، سرطان المبيض 35% ، سرطان عنق الرحم 6% ، ورم الأرومة الغاذية الحملي ( 8 GTN % ) ، وسرطان المهبل 2% . في حين كانت أعلى معدلات الإصابة بالمرض في الاعمارالاتية: سرطان الرحم والمهبل عند سن 50-59 سنة ( 73.5 % ، 50 % ) سرطان المبيض عند سن 40-49 سنة 42.9 % ، وسرطان عنق الرحم في سن 60-69 سنة 50 % . غالبية العمليات الجراحية التي خضع لها المرضي من قبل طبيبات النسائية والتوليد ( 62 % ) ، وخضع جميع المرضي تقريبا لعملية استئصال الرحم الكامل مع المبيضين وقناتي المبيض ( 92% BSSOO + TAH % ) مع فقط من الحالات كان استئصال العقد اللمفاوية في الحوض ( 2 % PLND ). تظهر متابعة لمدة عامين معدلات رجوع المرض بالنسب الاتية 32 % ، 28.6 % ، و 100

% لكل من سرطان الرحم والمبيض وسرطان عنق الرحم على التوالي. الخلاصة: يحدث سرطان النساء في الفئة العمرية

الأصغر سنا مع مرحلة عدوانية نسبيا وارتفاع معدل التكرار في محافظة كركوك.

الكلمات المفتاحية: سرطان النساء , PLND , كركوك

## 1- Introductions

Gynecological cancer consists of group of cancer that involve (uterus cancer, ovarian cancer, cervix uteri cancer, vaginal cancer, valval cancer and placenta site cancer) with most frequent site of cancer start from Endometrial comprising 6% of all cancers in women followed by Ovarian cancer in the second place and cervical cancer in the third place among women in the United States [1]. It is clear that an improvement in outcome of these malignancies can only be achieved if early diagnosis is achieved, there is accurate prediction of progression and response, and new treatment options reflecting the molecular pathogenesis and progression are developed [2].

In 1976, the American Joint Committee adopted the classification of the International Federation of Gynecology and Obstetrics (FIGO), which is the format used in the Annual Report on the Results of Treatment in Carcinoma of the Uterus, Vagina and Ovary, which is published every 3 years. This report has used the FIGO classification with periodic modifications since 1937, the last being 2009. Numerous institutions throughout the world contribute their statistics for inclusion in this voluntary collaborative presentation of data [3]. The TNM categories have therefore been defined to correspond to the FIGO stages. Some amendments have been made in collaboration with FIGO, and the classifications now published have the approval of FIGO, the American Joint Committee on Cancer (AJCC), and all other national TNM committees of the international union against cancer (UICC) [4].

Treatment of uterine and ovarian cancer have historically begun with surgical staging and cytoreduction. Thorough surgical staging is essential, as subsequent treatment will be based directly on the surgical stage. In ovarian cancer Cytoreduction, or debulking, refers to removing as much gross tumor as technically feasible. "Optimal cytoreduction" (now defined as  $<0.5$  cm largest residual tumor, or even better no gross visible residual disease) confers a significant survival advantage [5]. Low-risk endometrial cancer {Histologic grade 1 or 2, Cancer limited to the endometrium (a subset of stage IA disease), and Cancer that is not a high-risk histologic type (eg, clear cell, serous, or carcinosarcoma) Surgery is the standard treatment. Lymphadenectomy to be discussed in low risk patients. Sentinel node mapping could be performed but it is not a standard of care. For Intermediate-risk endometrial cancer (Cancer

confined to the uterus and invading the myometrium (a subset of stage IA or stage IB) or cancer that demonstrates occult cervical stromal invasion (stage II) excludes women with serous or clear cell cancers, which are considered to be high-risk histologic types regardless of the stage at presentation. A subset of women is considered to have high intermediate-risk based on certain pathologic criteria: 1-The Gynecologic Oncology Group (GOG) defines high intermediate-risk based on age and any of three pathologic factors: {1-the presence of deep myometrial invasion, grade 2 or 3 histology, or the presence of lymph vascular space invasion (LVSI). Women have high intermediate-risk disease if they are:  $\geq 70$  years with one risk factor, age 50 to 69 years with two risk factors, or age  $\geq 18$  years with all three risk factors Post-Operative Radiation Therapy in Endometrial Cancer (PORTEC) trials define high intermediate-risk by two of three clinicopathologic factors present: age  $> 60$  years, outer half myometrial invasion, and grade 3 histology [6]. Adjunctive RT in early stage intermediate risk endometrial carcinoma decreases the risk of recurrence, but should be limited to patients whose risk factors fit a high intermediate risk definition [7]. Surgical management is generally limited to patients with disease limited to the cervix or with limited involvement of the upper vagina. Depending on the clinical stage, fertility goals, and physical condition of the patient, surgical treatment ranges from cone excision of the cervix, to simple hysterectomy, to radical trachelectomy (where the cervix and parametria are removed with preservation of the uterine corpus), to radical hysterectomy [8]. The gestational trophoblastic neoplasia (GTN) refers to various histologic entities that have the ability to invade locally and/or metastasize. These conditions include persistent or invasive hydatidiform moles, placental site trophoblastic tumors, and choriocarcinomas [9]. GTN is a highly curable disease that can be effectively managed with single ethotrexate or actinomycin D) - or multiagent chemotherapy (EMA/CO protocol). Nonetheless, some women succumb from GTN primarily due to late presentation, delayed diagnosis of primary or recurrent disease, or drug resistance. Therefore, educating primary care physicians and gynecologists about the signs and symptoms of GTN is essential in decreasing adverse outcomes related to this disease. In addition, careful follow-up of all women with GTN is important to ensure that recurrence is detected promptly, at a time when it is curable. Moreover, the discovery of novel therapeutics may decrease drug toxicity, enhance treatment efficacy, and improve the management of women with chemo resistant disease [10]. Management of vulvar squamous cell and adenocarcinomas is wide radical excision (radical hemi/vulvectomy) with or without regional

lymph node dissection to radical vulvectomy with bilateral groin LN dissection or a pelvic exenteration for T4 tumor can be considered. Neoadjuvant combination chemotherapy and radiation therapy should also be considered for these advanced-stage patients Treatment for Stages II, III, and IV is definitive radiotherapy with concurrent platinum-based chemotherapy. treatment of vaginal cancer is consist of irradiation of groins with a radical hysterectomy with upper vaginectomy and LN dissection, or an upper vaginectomy and parametrectomy with LN dissection if the uterus has previously been removed. Radiation without surgery has equivalent outcome for tumor that involve the upper two-thirds of the vagina, it can include Concurrent platinum-based chemotherapy [11].

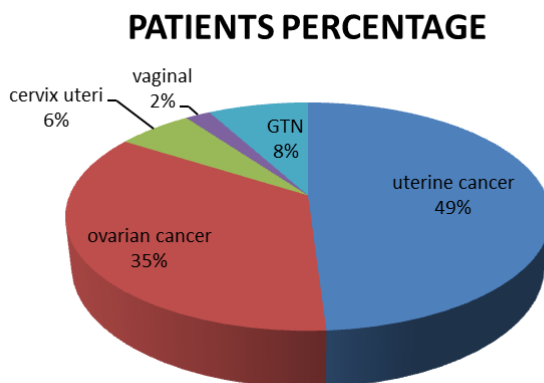
## 2- PATIENTS AND METHODS

It is retrospective-prospective observational study. The samples are collected from Kirkuk Oncology Center in period between 2016 November to 2018 August. A random selected sample of 100 female patients were diagnosed with cancer of genital tract and managed in the previous mentioned centers were and evaluated. Collected data included full questionnaire regarding (age and clinic-pathological assessment (such as cancer type, tumor size, histological type, lymph node status, TNM staging, and type of surgery and recurrence of disease). In addition, we followed those patients for any signs of recurrence during the 2-year time of our study in the center.

The first step of the data collection was general information collected from the hospital records via patient database provided in their files in the registry unit at the hospital. Completion of the full questionnaire for each patient was done during their requested visits to the hospital, either for receiving treatments and follow up sessions or merely for this study.

## 3- Results

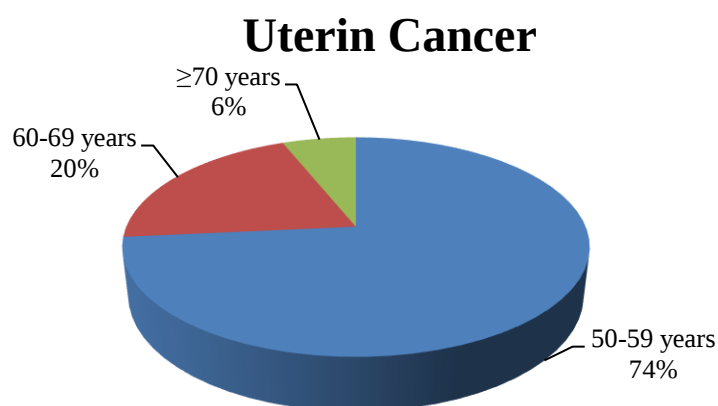
A total of 100 patients with gynecological cancer were reviewed in this study. As shown in Figure 1, uterine cancer accounts as 49%. Followed by ovarian cancer 35%, cervix cancer 6%, Gestational trophoblastic neoplasia GTN about 8%, and finally vaginal cancer 2%.



**Fig 1** Patents Distributions according to Gynecological Cancer Type

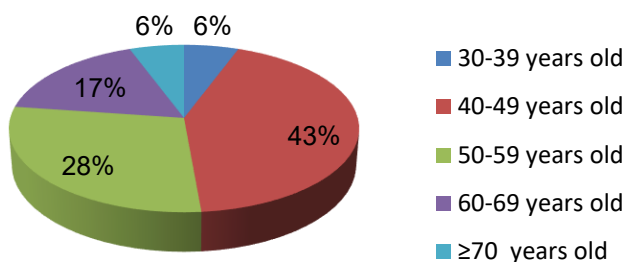
A total of 49 patients with uterine cancer were distributed according to their age. Three quarter of patients (no=36) were at age of (50-59 years old), about One fifth (no=10 patients) were at age (60-69) years old and only (6.1%, no=3) were above 70 years old as shown in figure 2.

Majority of patients with ovarian cancer (42.9 %, no=15 patients) were at age 40-49 years old, (28.6, no=10) were at age 50-59 years old and (17% no= 6) were at age 60-69 years old as shown in figure 3.



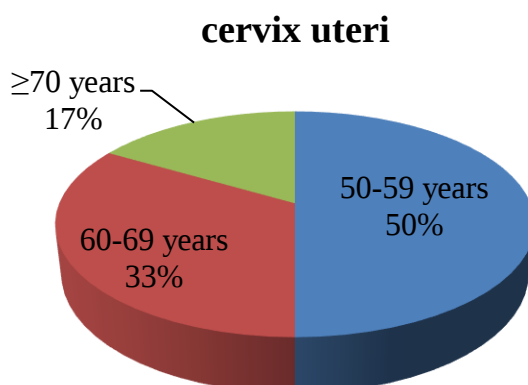
**Fig 2** Distribution of Patients with Uterine Cancer according to their Age.

## PATIENTS WITH OVARIAN CANCER



**Fig 3** Distribution of Patients with Ovarian Cancer according to their Age

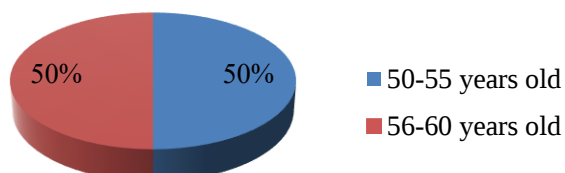
As shown in figure 4, half of the patients with cervix uteri cancer were at age 50-59 years old and about one third at age of 60-69 years old.



**Fig 4** Distribution of Patients with Cervix Uteri Cancer according to Age

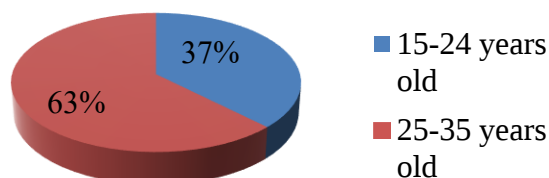
As illustrated in figures (5,6), patients with vaginal cancer were mainly presented at age above 50 years old, whereas patients with GTN were mainly presented between age group 20-35 years old (62%, no= 5).

### Vaginal cancer patients



**Fig 5** Distribution of Patients with Vaginal Cancer according to their Age.

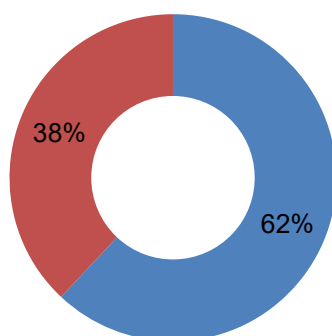
### Patients with GTN



**Fig 6** Distribution of Patients with GTN according to their Age.

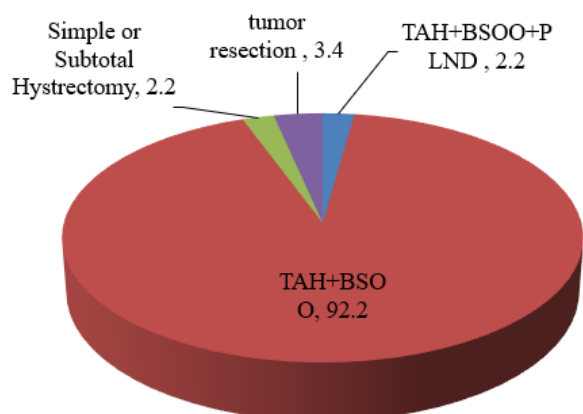
A total of two third of patents (No=62) their surgery was done by gynecological & obstetrician surgeons, and only one third (38), their surgery was done by general surgeons.

■ gynecologist &obstetrician surgeon ■ general surgeon



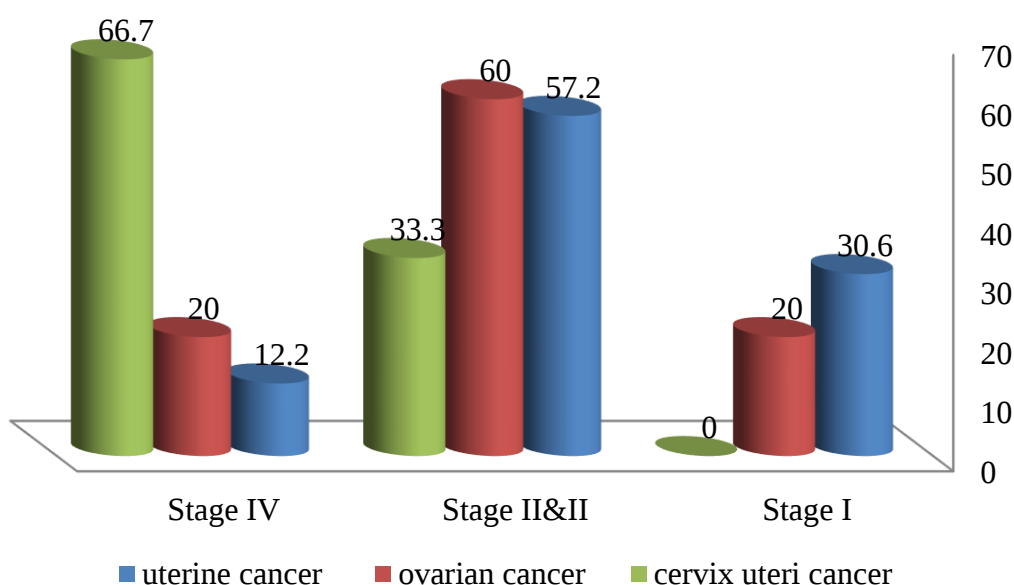
**Fig 7** Distribution of Patients according to Surgeon Specialty.

About 90 patients with (uterine cancer, ovarian cancer and cervix cancer) were reviewed. For the type of surgical procedure which was selected, the majority of them (92%, No=83) underwent TAH+BSOO and only (2.2% no=2) underwent TAH+BSOO+PLND. As showed in figure 7.



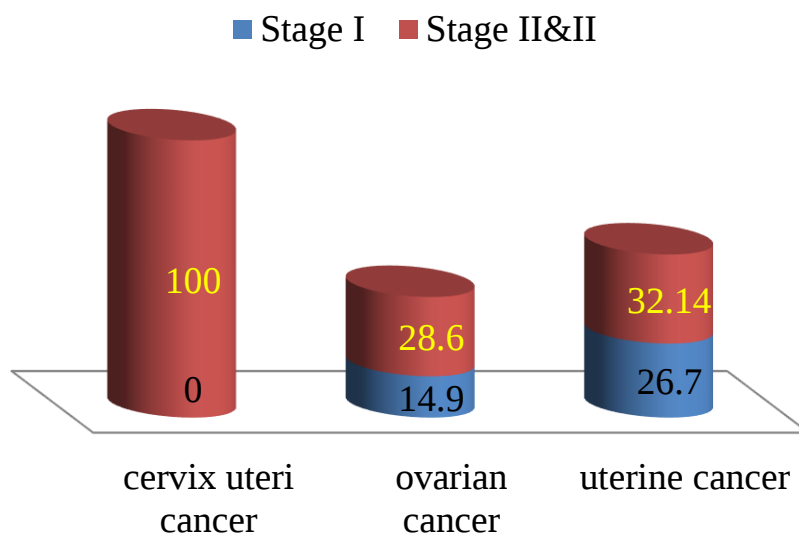
**Fig 8** Patients Distribution according to Type of Surgical Procedures in Patients with (uterine cancer, ovarian cancer and cervix. uterine cancer)

As shown in figure 9 , about two third of patients with uterine cancer (no=28 patients) were in stage II and III , two third of ovarian cancer patients were in stage (II ,III) (NO= 21%) and four fifth of patients with cervix cancer in stage IV of cancer .While there is only one third (15 patients)with uterine cancer in stage I , one quarter (7 patients) with ovarian cancer in stage I and about zero patients with cervix cancer in stage I.



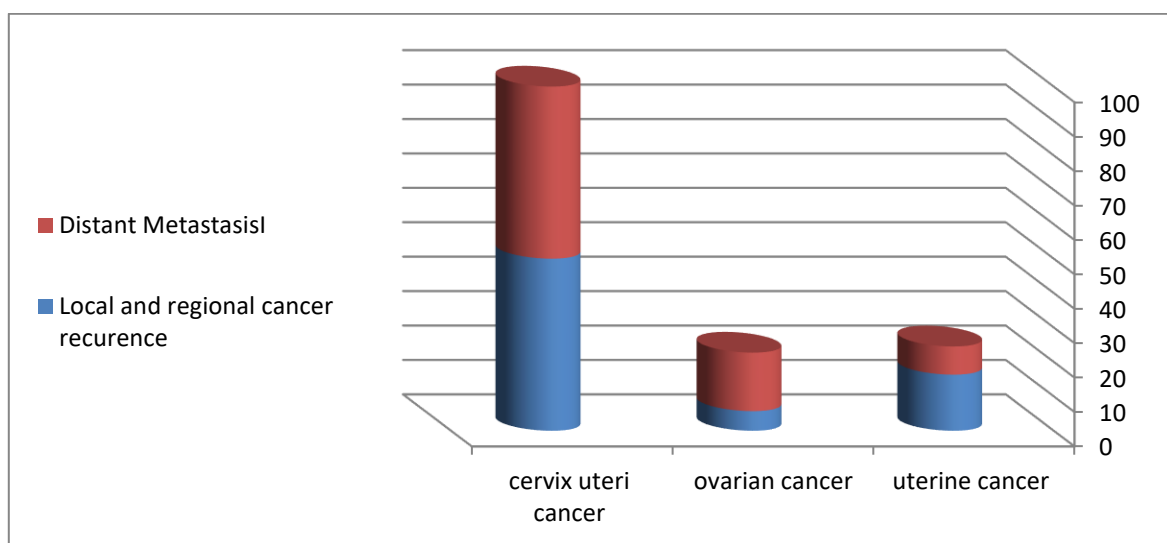
**Fig 9** Patients distribution according to disease stage and type of cancer

The reoccurrence rate for stage I uterine cancer were (26.7, no=4), ovarian cancer (32.14 no=1), while in sage II, uterine cancer (32.14 no=9), ovarian cancer (28.6 no=6) and (100% no =2) for cervix uterine as shown in figure 10.



**Fig 10** Patient Distributions according to Reoccurrence Rate for Stage II, I and III

As shown in figure 11, distribution of patients according to site of disease reoccurrence were as follows; for local metastasis, uterine cancer (16.3%, no=8), ovarian cancer (5.7%, no=2) and cervix at (50%, no=1). Distribution of patients with distant metastasis were: uterine cancer (8.1%, no=4), ovarian cancer (17%, no =6) and cervix uteri (50%, no=1).



**Fig 11** Patients Distribution according to Cancer Type and Site of Diseases Reoccurrence.

#### 4- DISSCUSIONS

Worldwide, Cervix uteri cancer is the most commonly diagnosed type of Gynecological cancer in 28 high developing countries (USA, Europe, and etc.) Followed by uterine cancer in second place and ovarian cancer in third place [11]. In this study, uterine cancer found to be most frequent gynecological cancer. Gynecological cancer occupies about 50% of the cases followed by ovarian cancer 30% of the cases and finally, cervical cancer about only 6% .

Screening program for both ovarian and cervical cancer, were well established worldwide due to high incidence of the previously mentioned cancers and relatively high sensivity rate of these test. Screening for cervical cancer in high developed countries utilize screening for The HPV (human papilloma virus) with a Pap smear in early sexually active female (between ages 21 -29 years) [12]. The UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS), use transvaginal ultrasound and annual CA-125 test as screening tool in women between ages of 50-74years [13]. Peak age incidence of Cervical cancer is most frequently diagnosed in women between the ages of 35 -44. It rarely develops in women younger than 20 years old [14]. Also, according to Globe can data the Peak age incidence of uterine cancer in United Kingdom is age group (75-79years old), [15] while incidence peak age in our study, is age group 50-59 years old. Ovarian cancer rates are highest in women age 55-64 years about one quarter of the case [16]. Albeit in our population, the peak age incidence is-age group 40-49 years old.

Surgical treatment of ovarian cancer, including systematic lymphadenectomy, should be performed only at gynecologic oncology specialized institutions in order to ensure accurate staging of the tumor. According to the data from the Japan Society of Obstetrics and Gynecology tumor registry (2012), pelvic and para-aortic node dissection are currently performed only for about 40% of patients with early stage ovarian cancer in Japan [17].

In an Italian study of over 500 patients with stage I endometrial cancer demonstrated no difference between those patients who underwent lymphadenectomy and those who did not. Disease-free survival was 80% in the lymphadenectomy group compared to 82% in the no lymphadenectomy group [18]. The Italian study was criticized for a disproportionate use of adjuvant treatment in the no lymphadenectomy group and the 16% of patients randomized to

lymphadenectomy actually had lymph nodes removed. Evaluation of over 12,000 patients from the Surveillance, Epidemiology and End Results (SEER) database found an improved 5-year disease specific survival with lymphadenectomy in stage IB grade 3 and higher [19].

With the thought that lymphadenectomy may be of benefit in the higher risk group, the GOG has proposed a prospective trial to evaluate the role of lymphadenectomy in high risk patients [20].

In contrary, in this study only 2% of patients underwent pelvic lymph node dissection with total abdominal hysterectomy and bilateral salpingo-oophorectomy. This might be one of the causes of relatively high 2 years reoccurrence rate about 36% in uterine cancer, 45% ovarian cancer and 100% in cervical cancer. On the other hand, Korean studies show only 14% recurrence rate in patients with endometrium cancer underwent TAH+BSOO+PLND [21]. According to Japanese study, the 2 years reoccurrence rate of ovarian cancer in spite of recent progress in treatment strategy, is still the leading cause of death among cases of gynecologic cancer. Generally, 70% of advanced stage of ovarian cancers relapse even in stage I or II patients. The relapse rate is 20%–25% [22]. According to Thailand study, the reoccurrence rate of cervical cancer was comparable with this study; approximately, half of the reoccurrences were mostly local and distant metastasis cases encountered in 49.3% [23].

## 5- Conclusions:

There is a great difference in demographical characteristic of gynecological cancer in Kirkuk city. It was presenting in younger age group patients with relatively aggressive stage and high recurrence rate. This requires paying attention to establish our own applicable treatment guideline.

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