RESEARCH ARTICLE

Proportion of Ovarian Cancers in Overall Ovarian Masses in Thailand

Yada Kunpalin*, Surang Triratanachat, Patou Tantbirojn

Abstract

Background: The primary objective of this study was to assess the proportion of malignancies in ovarian masses during 1st January 2002, to 31st December 2011 at the Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital. A secondary objective was to evaluate associations with patients' clinical characteristics and ovarian malignancy proportion and subtypes. Materials and Methods: Retrospective descriptive study analyzed data of ovarian masses larger than 3 centimeters in maximal diameter, from the division of Gynecologic Cyto-Pathology at KCMH. SPSS software version 17 (SPSS, Inc, Chicago, IL, USA) was used. Results: A total number of 6,115 patients were included. Among the total ovarian masses studied, 13.7% were malignant. After the age of sixty, the proportion reached almost 40%. It was also above 20% in women younger than 20 years old. During premenarche period, proportion of ovarian malignancies was 50%. Only 1% of ovarian masses were found to be malignant during the pregnancy and post-partum periods. Parity decreasedthe probability of ovarian malignancy during postmenopausal years. Period of menopause did not have any impact on this probability. During the first two decades of life, germ cell malignancy dominated. As the age increased, the percentage of surface epithelial-stromal malignancy increased with a peak at the fifth decade. In contrast, malignant sex cord-stromal cell tumors occurred at a constant rate in each age group after the thirties. Conclusions: Proportion of ovarian cancers in each age group, menstrual and pregnancy status are similar. However there are differences in the distribution of ovarian subtypes especially for the surface epithelial-stromal category.

Keywords: Ovarian masses - ovarian cancers - pregnancy - menopause - Thailand

Asian Pac J Cancer Prev, **15 (18)**, 7929-7934

Introduction

Ovarian cancer is the second most common gynecologic cancer found in Thai women behind only cervical cancer. The age-standardized incidence rate of ovarian cancer in Thailand was 6.2 per 100,000 population (Khuhaprema et al., 2013), which is comparable to that worldwide (Ferlay et al., 2013). The incidence rate of cervical cancer has shown a downward trend owing to the effectiveness of its screening program. On the other hand, the incidence rate of ovarian cancer is gradually increasing especially in Asian countries (Murthy et al., 2009; Bing et al., 2014) as there is currently no accurate screening test available for early ovarian cancer detection and clinical presentations are very subtle early in the disease. Therefore patients are more likely to be diagnosed with advanced stages of the disease with poor prognosis (Cancer Facts & Figures 2014). This accounts for it being the leading cause of death amongst all gynecologic cancers in developed countries including Thailand with an estimate of 151, 905 deaths a year worldwide (Khuhaprema et al., 2013).

Since our institutional study on primary ovarian lesions was conducted over a decade ago, new data should be collected in order to verify findings in the previous study. The primary objective of this study was to assess the proportion of malignancy in ovarian masses using data collected from 1st January 2002, to 31st December 2011 at the Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital. The secondary objective was to evaluate whether there is any association between patients' clinical characteristics (such as age, premenarche, pregnancy status and menopausal conditions) and ovarian malignancy. Recent study (Sung et al., 2014) have found that prevalence of different subtypes of ovarian cancer found in Asian countries are significantly different from that found in the West. Thus the last objective of this study is to see if our data reflect similar findings.

Materials and Methods

We conducted a retrospective descriptive study analyzing data from the division of Gynecologic Cyto-Pathology at KCMH. This study was approved by the Institutional Review Board, the Faculty of Medicine,

*Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand *For correspondence: Yada.kunpalin@gmail.com*

Chulalongkorn University.

We were able to have access to data of ovarian specimens, which were collected from patients undergoing oophorectomy or cystectomy between 1st January 2002, to 31st December 2011 at the Department of Obstetrics and Gynecology, KCMH.

We decided to select ovarian masses that were recorded as larger than 3 centimeters in maximal diameter. Formalin-fixed paraffin blocks and pathologic glass slides were obtained with the patients' demographic information (including age, pregnancy status, and menopausal conditions) collected. Specimens were excluded if patients' information or pathologic evidence could not be retrieved. The previously made diagnoses were reviewed by gynecologic pathologists. In the event that the diagnosis did not correlate, the specimen will be re-evaluated by gynecologic pathologists to reach consensus on the final diagnosis. The diagnosis was made according to the WHO classification for tumors of the breast and female genital organs, IARC PRESS, Lyon, 2003.

A statistical analysis was leveraged by SPSS software version 17 (SPSS, Inc, Chicago, IL, USA). The pathologic data and patients' characteristics were compared by descriptive statistics. Pearson's chi-squared test was used to determine if there is ant statistical difference in categorical data.

Results

A total number of 6, 115 patients who had ovaries removed satisfied the defined criteria and subsequently were included in the study. Demographic data is shown in Table 1. Age of the patients ranged from 6 to 93 years old with the mean age being 41 years old (SD±11.5 years). Half of the included populations were nulliparous. Reproductive age group formed almost 85% of the patients in the study.

The proportion between benign and malignant tumors in each ovarian category is shown in Figure 1. Surface epithelial-stromal malignancies accounted for 45% of epithelial neoplasms. Sex cord-stromal and germ cell malignancies affected only 26% and 6.5% of each category respectively. Majority of ovarian malignancies were surface epithelial-stromal tumors, which occupied 81% of the whole ovarian malignancies. Only 3.3% and 6% of ovarian malignancies were diagnosed as sex cord-stromal and germ cell malignancies respectively. In our study, 9.7% of ovarian malignancies were metastasis. Most common sites of primary tumors were other genital tract malignancies (41.1%), gastrointestinal tract malignancies (24.1%) and unknown sites (28.9%).

Figure 2 demonstrates the proportion of ovarian malignancy in each age group. In the elderly age group, the proportion of ovarian malignancy reached almost 40%. The proportion of malignancy was above 20% in children and teenagers but on 5-10% in reproductive age women. Furthermore, the proportion of tumors with low malignant potential was relatively constant at a percentage of 1.5-7.5% in across all age groups.

Figure 3 shows the proportion of each pathologic subtypes of ovarian malignancy. During the first two decades of life, germ cell malignancy dominated. As the

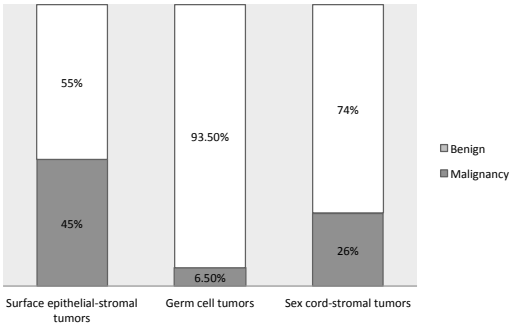

Figure 1. Proportion of Ovarian Malignancy in Each Category

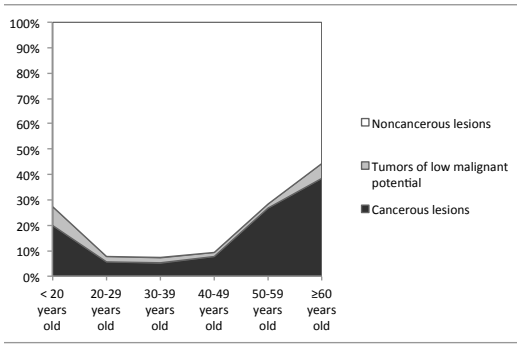

Figure 2. Proportion of Ovarian Malignancy in Each Age Group

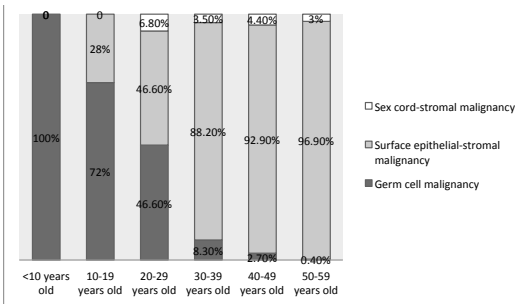

Figure 3. Proportion of Each Pathologic Subtypes of Ovarian Malignancy

Table 1. Demographic Data

Demographic data	Frequency	Percentage (%)
Age (years old)		
< 20	95	1.6
20-29	788	13
30-39	1,761	28.7
40-49	2,255	36.9
50-59	847	13.8
≥ 60	369	6.0
Number of pregnancy		
Nulliparas	3,241	53
1	930	15.2
2	840	13.7
≥ 3	569	9.3
Unknown	535	8.8
Patients' status		
Premenarche	10	0.2
Reproductive age	5,201	85
(Pregnancy)	289	
Postmenopause	904	14.8
Total	6,115	100%

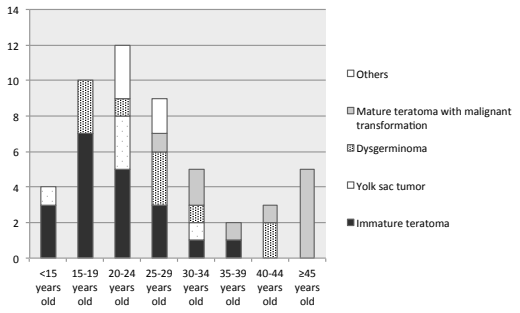

Figure 4. Distribution of Germ Cell Malignancies by Age Groups

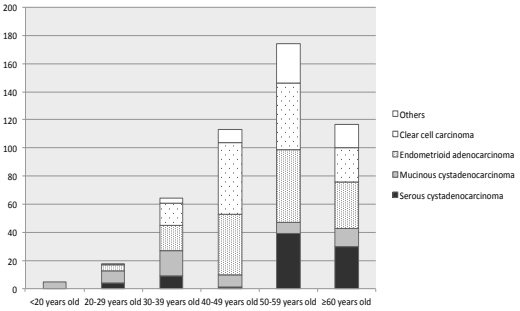

Figure 5. Distribution of Surface Epithelial-Stromal Malignancies by age Groups

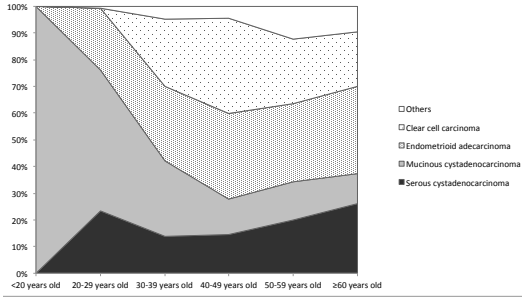

Figure 6. Distribution of Subtypes of Surface Epithelial-Stromal Malignancies by Age Groups

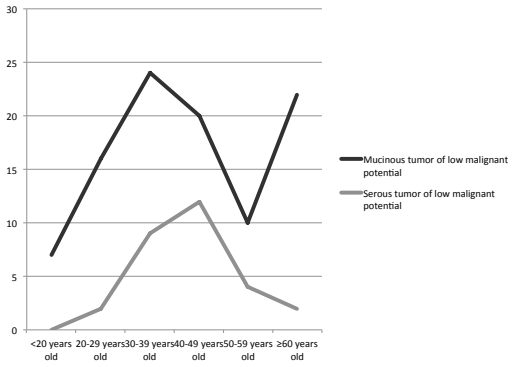

Figure 7. Distribution of Surface-Epithelial Tumors of Low Malignant Potential

age increased, the percentage of surface epithelial-stromal malignancy increased with a peak at the fifth decade. In contrast, malignant sex cord-stromal cell tumors occurred at a constant rate in each age group after the thirties. Interestingly, the only germ cell malignancy found after the age of 40 was mature teratoma with malignant transformation.

In our study, germ cell malignancies were diagnosed in 50 patients with age ranged from 6-71 years old. Tumor distribution by age groups was shown in Figure 4. This subtype is most common during the first three decades of life with its peak in the twenties. After the fourth decade, only mature teratoma with malignant transformations was identified, 60% of which were squamous cell carcinoma.

Surface epithelial-stromal cancer was diagnosed in 542 patients with age ranged from 13-93 years old. Its proportion increased with age with its peak in the fifties as shown in Figure 5. With increasing age the proportion of endometrioid adenocarcinoma and clear cell carcinoma substantially increased. Using 40 years of age as a cut-off point, there is significant difference in the proportion of clear cell carcinoma found in women before and after 40 years of age (8.3% *vs* 26.6%, p=0.004), but not in endometrioid adenocarcinoma. However the proportion of mucinous cystadenocarcinoma was trending down and there is significant difference when using 40 years of age as a cut-off point (37.0% *vs* 13.2%, p<0.001). Moreover, the proportion of serous cystadenocarcinoma was relatively constant across all age groups (15-25%) as shown in Figure 6.

Figure 7 shows the distribution of mucinous and serous tumors of low malignant potential. Mucinous type is predominately identified in each age group in our studies with peak incidence during the third and fourth decades.

A total number of 289 pregnant and postpartum women were identified as having ovarian masses larger than 3 centimeters. Age was ranged from 17-49 years old with the mean age of 31 years old (SD±5.7 years). Only 1% (3/289) of ovarian masses was found to be malignant and another 2% (6/289) were tumors of low malignant potential. For malignant lesions, only two subtypes (epithelial-stromal and metastatic ovarian malignancies) were found in this group. Interestingly, mucinous cystadenocarinoma is the only epithelial-stromal subtype being found. For tumor of low malignant lesions, all of which were mucinous subtype.

Only 10 ovarian specimens were identified in premenarche, 50% of which were malignant. All of these were classed as germ cell malignant with immature teratoma predominating (30%).

A total number of 904 postmenopausal women were found to have ovarian masses larger than 3 centimeters. Age was ranged from 45-93 years old with the mean age of 59.7 years old (SD±8.55 years). The proportion of ovarian malignancies was 40% in this extreme age group.

There is significant difference in the proportion of ovarian malignancies found in pregnant and postpartum women when compared to that in non-pregnant reproductive women (1.0% *vs* 8.6%, p<0.001) This significant difference was also seen when making comparison between premenarche and non-pregnant reproductive women (50% *vs* 8.6%, p<0.001)) However the difference is no longer significant when comparing two extreme age groups (premenarche and postmenopause) (50% *vs* 40%, p=0.54).

Parity decreases the probability of ovarian masses being malignant (58% *vs* 38%, p<0.001) during

Table 2. Histologic Subtype

Ovarian pathological diagnosis	Frequency	Percentage
Tumor-like conditions	2534	2459
Endometriotic cyst	41.4	40.2
Oophoritis, ovarian abscess	67	1.1
Others	8	0.1
Surface epithelial-stromal tumors	1493	486
Serous cystadenoma	24.4	8.0
Mucinous cystadenoma	317	5.2
Endometrioid adenocarcinoma	150	2.5
Clear cell carcinoma	138	2.3
Serous cystadenocarcinoma	104	1.7
Mucinous tumor of low malignant potential	99	1.6
Mucinous cystadenocarcinoma	92	1.5
Mixed epithelial tumor	51	0.8
Serous tumor of low malignant potential	29	0.4
Others	27	0.4
Functional ovarian cysts	1114	616
Follicle cyst	18.2	10.1
Corpus luteal cyst	485	7.9
Others	13	0.2
Germ cell tumors	767	717
Mature teratoma	12.6	11.7
Immature teratoma	20	0.3
Dysgerminoma	10	0.2
Mature teratoma with malignant transformation	10	0.2
Yolk sac tumor	6	0.1
Others	4	0.1
Sex cord-stromal tumors	120	78
Fibroma	1.9	1.3
Adult granulosa cell tumor	27	0.4
Thecoma	7	0.1
Others	8	0.1
Secondary tumors	80	1.4
Miscellaneous, lymphoid and hematopoietic tumors	7	0.1
Total	6,115	100

Table 3. Factors Affecting Ovarian Cancer Proportion in Postmenopausal Women

Comparing factors	Percentage	P value
Nulliparous postmenopausal women	58%	38%
Parous postmenopausal women	<0.001	
Within 10 years, postmenopausal women	43.5%	44.3%
More than 10 years, postmenopausal women	0.58	

postmenopausal years. Period of menopause does not have any impact on this probability when comparing women having menopause less than 10 years and those more than 10 years (43.5% *vs* 44.3%, p=0.58) as shown in Table 3. However, postmenopause status was found to increase this probability when comparing women aged between 45 and 55 yeas old with menstruation and those without (10.2% *vs* 38.8%, p<0.001).

Discussion

In our study, the proportion of ovarian cancer in overall ovarian masses was 13.7%. The proportion increased in extreme age groups: children, teenager and postmenopausal women. Ovarian masses found in children and teenagers had 20% risk of malignancy in our study. This number is similar to that of a literature review, which found from that 33% of childhood ovarian tumors were malignant (Breen et al., 2008). After the fifth decade, discovered ovarian masses in our study had 32.7% risk of malignancy. This finding is well correlated with the peak incidence of ovarian cancer worldwide, which occurs during the fifth decade in women's life. Nonetheless, the proportion of ovarian cancer in women aged between the second and fifth decades of life fall dramatically, owing to an increase in the incidence of functional cysts, mature cystic teratomas and endometriotic cysts.

Alongside with age, we also found that menstrual status had an effect on malignancy development of recognized ovarian masses in premenarche (50%) and postmenopausal (40%) women since ovaries in these females are quiescent and the presence of palpable ovarian masses must alert physicians for a possibility of malignancy. These two groups shared roughly the same risk of ovarian malignancy. Our study showed that the proportion of ovarian malignancy slightly increased across menopausal years but did not reach statistical significance. This contradicts with a common belief that the higher the number of years after menopause the higher the chance of having ovarian malignancy. Predictably, parity is considered to be a protective factor for ovarian cancer in postmenopausal women. From our findings, only one successful live birth significantly reduced the proportion of ovarian cancer in postmenopausal women. The strong protective association of parity for ovarian cancer development has been well establish in other studies (Tsilidis et al., 2011; Gao et al., 2012). We found that the proportion of ovarian cancer in ovarian masses is smaller in pregnant women than in general reproductive age women. One percent of removed ovarian masses found in pregnant women were malignant, which is coincides with a previous review conducted in North America (Leiserowitz et al., 2006). In most studies, germ cell tumors accounts for the majority of ovarian malignancies in pregnant women. However, in our study only epithelial ovarian malignancy is the only type found in pregnant women. This may due to a delay of childbearing and a small number of the studied population in our study.

From our findings, ovarian tumors composed of 4.9% of sex cord-stromal subtype, which is comparable to our previous institutional study (4.1%) (Trivijitsilp et al., 1999) but less than studies conducted worldwide (8%) (Tavassoli et al., 2003). Majority of the cases were benign in origin with fibroma being the most commonly diagnosed tumor. Almost all of malignant subtype was adult granulosa cell tumor covering 3.3% of all ovarian malignancies or 0.4% of all ovarian tumors. This proportion is similar to the proportion of sex cord-stromal cancers among Thai women across the country (2-8%) but slightly lower than our previous institutional data (5.2%) (Trivijitsilp et al., 1999). These findings indicated that the proportion of sex cord-stromal tumors were relatively constant with time and ethnicity. In our study, there was no case of granulosa cell tumor diagnosed before the age of twenty or of juvenile subtype. These findings are consistent with other studies that granulosa cell tumor is a rare malignancy before the second decade of life (Haroon et al., 2013) and juvenile subtype commonly affects prepubertal and young female patients (Haroon et al., 2014). These young patients commonly seek for medical advice from pediatrics surgery department and therefore were not included in our study. Adult granulosa cell tumor constantly affects women across a wide range of ages

especially during perimenopausal or early postmenopausal periods (Schumer et al., 2003). This is well reflected in our findings.

Germ cell tumors comprised 31.1% of all ovarian tumors in our study. This proportion is consistent with reports from West countries (30%) (Tavassoli et al., 2003) but less than our previous data (46.8%)(Trivijitsilp et al., 1999) and reports from other Asian countries (39.5-43.36%) (Nakashima et al., 1990; Sah et al., 2004). This indicates that germ cell tumors were less frequently encountered in our institution from time to time. Our previous institutional data revealed that 45.3% of ovarian tumors were mature teratoma (Trivijitsilp et al., 1999). In contrast, our finding showed that mature teratoma accounted for 29.1% of ovarian tumors. This may explain a smaller proportion of germ cell tumors found in our study. Almost all of the diagnosed germ cell tumors (93.5%) were mature teratoma. The number is close to our previous data (95.3%) (Trivijitsilp et al., 1999), data from Nepal (93.39%) (Sah et al., 2004) and western countries (95%) (Tavassoli et al., 2003). This is similar to that found in other countries (3-14%) but slightly lower than our previous institutional data (9.85%). This malignancy mostly affected children and adolescent females, especially before the forth decade. From our findings, the only malignant type affected women older than 45 years old were mature teratoma with malignant transformations (squamous cell carcinoma being the most commonly identified), one of the most serious complications of mature teratoma. This accounts for 1.4% of all diagnosed mature teratoma in our study, which correlated with other studies (Sakuma et al., 2010; Oranratanaphan et al., 2013). Additionally immature teratoma was the most common germ cell malignancy in our study. This is consistent with the finding from a study in South Korea (Lee et al., 2009). However, most studies and our previous data reported that dysgerminoma was the most common germ cell malignancy (Trivijitsilp et al., 1999; Tavassoli et al., 2003; Lertkhachonsuk et al., 2005; Cicin et al., 2009; Tangjitkamol et al., 2010). Although different types of germ cell malignancy may vary in proportion from study to study, immature teratoma, dysgerminoma and yolk sac tumor are always the three most common malignant subtypes.

From our study, surface epithelial-stromal tumors accounted for 60.5% of ovarian tumors, the highest proportion of all ovarian subtypes. This number is much higher than our previous data (47.4%) (Trivijitsilp et al., 1999) owing to a decrement in the proportion of germ cell tumor. Epithelial ovarian malignancy accounted for 81% of all ovarian malignancies. Endometrioid adenocarcinoma (27.6%) and clear cell carcinoma (25.4%) were the two most commonly encountered subtypes in our study. The proportion of endometrioid adenocarcinoma in epithelial ovarian subtype is consistent with our previous data (28.5%)(Trivijitsilp et al., 1999). In contrast, these numbers are higher than those found in Thai country (11.8%)(Khuhaprema et al., 2013) and worldwide (12.6%) (Sung et al., 2014). In this study, clear cell carcinoma accounted for 13.6% of epithelial ovarian malignancy and this is higher than our previous data (13.6%) (Trivijitsilp et al., 1999). This is also higher than data from across the country (16%) (Khuhaprema et al., 2013) and worldwide (5.3%) (Sung et al., 2014). The proportion of clear cell carcinoma significantly increased after the fourth decade in our study. This finding is similar to data from a study in Japan that clear cell carcinoma is more frequent comparing to incidence in Western countries (Yoshikawa et al., 2014). Serous cystadenocarcinoma comprised 19.2% of ovarian epithelial cancers in our study. The number is less than our previous data (30.3%) (Trivijitsilp et al., 1999), Thai data (19.4%) (Khuhaprema et al., 2013) and worldwide (45%) (Sung et al., 2014). In our study, proportion of serous cystadenocarcinoma remains relatively constant across all age groups. However, mucinous cystadenocarcinoma, which accounted for 17% of ovarian epithelial malignancy, was more prevalent in younger women (age<40 years old) in our study. This value is similar to a study conducted in Japan, which indicated that mucinous cystadenocarcinoma is more frequent in patients aged ≤40 years (36.7%) (Yoshikawa et al., 2014). Proportion of mucinous cystadenocarcinoma is relatively the same as our previous data (20.3%) (Trivijitsilp et al., 1999) and that from country data (16.3%) (Khuhaprema et al., 2013). However, this is higher than the average worldwide (11.4%) (Sung et al., 2014).

The discrepancy of our statistics from data from across the country could be due to the distorted patient sampling as KCMH is a tertiary care center. In contrast, the differences of our data from worldwide value might indicate that there are some unique genetic and ethnic variations predisposing Thai women to certain ovarian pathological subtypes.

Since our hospital is a tertiary care center, the patients sampled might not reflect general Thai female population. This is considered to one of major limitations. Furthermore, another limitation is that there were a number of removed ovarian masses in other surgical departments that were not included in our study. Therefore, this could also distort the data and lead to underestimation of ovarian masses during childhood and metastatic ovarian tumors. In addition, this study is a retrospective study; its nature might cause error.

In conclusion, the proportion of ovarian cancers in each age group, menstrual and pregnancy status are similar in each ethnicity. However there are differences in the distribution of ovarian subtypes especially for the surface epithelial-stromal category. This is to emphasize that pathology subtypes of the ovarian cancers are inconsistent across different regions in the world and it may reflect distinct features of Thai and Asian populations.

References

American Cancer Society (2014). Cancer facts and figures Atlanta, 17-8.

Breen J, Denehy T (2008). Pediatric ovarian malignancies. Glob. libr. women's med, (ISSN: 1756-2228); DOI 10.3843/GLOWM.10251.

Cicin I, Eralp Y, Saip P, et al (2009). Malignant ovarian germ cell tumors: a single-institution experience. *Am J Clin Oncol*, **32**, 191-6.

Ferlay J, Soerjomataram I, Ervik M, et al (2013). Globocan 2012 v1.0, cancer incidence and mortality worldwide: IARC cancerbase no. 11. Lyon, France: International agency for

research on cancer, 2013
Gao S, Liu N, Ma Y, et al (2012). Methylenetetrahydrofolate reductase gene polymorphisms as predictive and prognostic biomarkers in ovarian cancer risk. *Asian Pac J Cancer Prev*, **13**, 569-73.
Gurung A, Hung T, Morin J, et al (2013). Molecular abnormalities in ovarian carcinoma: clinical, morphological and therapeutic correlates. *Histopathology*, **62**, 59-70.
Haroon S, Idrees R, Zia A, et al (2014). Ovarian sex cord stromal tumours in children and young girls-a more than two decade clinicopathological experience in a developing country, Pakistan. *Asian Pac J Cancer Prev*, **15**, 1351-5.
Haroon S, Zia A, Idrees R, et al (2013). Clinicopathological spectrum of ovarian sex cord-stromal tumors; 20 years' retrospective study in a developing country. *J Ovarian Res*, **6**, 87.
Khuhaprema T, Attasara P, Sriplung, H, et al (2013). Cancer in Thailand Vol. VII 2007-2009. ministry of public health, Bangkok, Thailand.
Lee K H, Lee I H, Kim B G, et al (2009). Clinicopathologic characteristics of malignant germ cell tumors in the ovaries of Korean women: a Korean gynecologic oncology group study. *Int J Gynecol Cancer*, **19**, 84-7.
Leiserowitz G S, Xing G, Cress R, et al (2006). Adnexal masses in pregnancy: how often are they malignant? *Gynecol Oncol*, **101**, 315-21.
Lertkhachonsuk R, Termrungruanglert W, Vasuratna A, et al (2005). Malignant ovarian germ cell tumor in King Chulalongkorn memorial hospital. *J Med Assoc Thai*, **88**, 124-8.
Murthy N S, Shalini S, Suman G, et al (2009). Changing trends in incidence of ovarian cancer-the Indian scenario. *Asian Pac J Cancer Prev*, **10**, 1025-30.
Nakashima N, Nagasaka T, Fukata S, et al (1990). Study of ovarian tumors treated at Nagoya University Hospital 1965-1988. *Gynecol Oncol*, **37**, 103-11.
Oranratanaphan S, Khemapech N (2013). Characteristics and treatment outcomes of patients with malignant transformation arising from mature cystic teratoma of the ovary: experience at a single institution. *Asian Pac J Cancer Prev*, **14**, 4693-7.
Sah S P, Uprety D, Rani S (2004). Germ cell tumors of the ovary: a clinicopathologic study of 121 cases from Nepal. *J Obstet Gynaecol Res*, **30**, 303-8.
Sakuma M, Otsuki T, Yoshinaga K, et al (2010). Malignant transformation arising from mature cystic teratoma of the ovary: a retrospective study of 20 cases. *Int J Gynecol Cancer*, **20**, 766-71.
Schumer S T, Cannistra S A (2003). Granulosa cell tumor of the ovary. *J Clin Oncol*, **21**, 1180-9.
Sung P L, Chang Y H, Chao K C ,et al (2014). Global distribution pattern of histological subtypes of epithelial ovarian cancer: a database analysis and systematic review. *Gynecol Oncol*, **133**, 147-54.
Tangjitgamol S, Hanprasertpong J, Manusirivithaya S, et al (2010). Malignant ovarian germ cell tumors: clinico-pathological presentation and survival outcomes. *Acta Obstet Gynecol Scand*, **89**, 182-9.
Tavassoli FA, Devilee P, et al (2003). Pathology and genetics of tumours of the breast and female genital organs. world health organization classification of tumours. IARC press: Lyon, 113-96.
Trivijitsilp P, Trirattanachart S, Niruthisard S, et al (1999). The frequency of primary ovarian neoplasms at King Chulalongkorn Memorial Hospital during 1990-1997. *Chula Med J*, **43**, 213-24.
Tsilidis K K, Allen N E, Key T J, et al (2011). Oral contraceptive use and reproductive factors and risk of ovarian cancer in the European prospective investigation into cancer and nutrition. *Br J Cancer*, **105**, 1436-42.
Wang B, Liu S Z, Zheng R S, et al (2014). Time trends of ovarian cancer incidence in China. *Asian Pac J Cancer Prev*, **15**, 191-3.
Yoshikawa N, Kajiyama H, Kikkawa F, et al (2014). Clinicopathologic features of epithelial ovarian carcinoma in younger *vs*. older patients: analysis in Japanese women. *J Gynecol Oncol*, **25**, 118-23.