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HACETTEPE UNIVERSITY

INSTITUTE OF HEALTH SCIENCES

REPRODUCTIVE CANCER RISK FACTORS AMONG RELATIVES OF CANCER PATIENTS SEEKING TREATMENT IN HACETTEPE UNIVERSITY ONCOLOGY HOSPITAL

Dr. Nooria ATTA

Cancer Epidemiology Program

MASTER of SCIENCE THESIS

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THESIS SUPERVISOR

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APPROVAL

This dissertation has been approved by the committee above in conformity to the regulations and bylaws of Hacettepe University Graduate Programs and has been accepted by the Board of Directors of the Institute of Health Sciences.

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ÖZET

Nooria, A. Hacettepe Üniversitesi Onkoloji Hastanesinde tedavi alan kanser hastalarının yakınları arasında jinekolojik kanser risk faktörleri. Hacettepe Ünıversitisi Sağlık Bilimler Enstitüsü Kanser Epidemiyoloji Programı Yüksek Lisans Tezi, Ankara, 2014. Bu çalışma, kanserli hastaların kadın akrabalarındaki üreme ile ilgili bazı spesifik kanser risk faktörlerini belirlemek için yapılmıştır. Prevantif Onkoloji Anabilim Dalı tarafından bir risk değerlendirme anketi hazırlandı. 2007 ve 2012 yılları arasında toplanan verile kullanıldı. Anket katılımcıların kendisi tarafından doldurulduu. Çalışmaya katılanların ortalama yaşı 45.7±12.2 idi. Ortanca menarş yaşı 13 yaş (IQR, 12-14) idi. Kadınların %6.9'u 12 yaşından önce menarş olduklarını bildirdi. İlk doğum sırasında ortanca yaş 22 idi. Ortanca vücut kitle indeksi 24.9 iken katılımcıların %18.3'ü obezdi. Kadınların %65'i geçmişte veya günümüzde sigara içmekteydi. Katılımcıların yaklaşık %11'i ilk cinsel temas yaşlarının 18 yaş ve öncesinde olduğunu belirtti. Çalışmadaki kadınların sadece %2.5'i yaşamları boyunca en az bir kez cinsel yolla bulaşan bir hastalığı olduğunu ifade etti. Yüzde 62 kadın hiç kondom kullanmadığını, %8'i mamografi ve %17.7'si Pap testi hakkında bilgisi olmadığını belirtti. Türkiye'deki genel popülasyonla karşılaştırıldığında çalışmaya katılan kadınlar daha ileri yaştaydı. Üreme ile ilgili kanser risk faktörlerinin prevalansı literatürdeki verilerle uyumlu idi. Mamografi hakkındaki kadınların farkındalık ve davranışları Pap testi ile karşılaştırıldığında daha iyiydi. Ayrıca insanların farkındalığını arttırmak ve kanser tarama çalışmalarına yönelik hastaların davranışlarını değiştirmek gerekmektedir. Kanser prevansiyonu amacıyla insanların yaşam-tarzı değişikliği yapmaları gerekmektedir. Bulgular Türk toplumunda kansere ait risk faktörlerini değerlendirmek için toplumu kapsayan daha fazla çalışmaya gereksinim vardır.

Anahtar kelimeler: Jinekolojik kanser, risk değerlendirme, risk faktörü, kanserde erken tanı, kanser taraması.

ABSTRACT

Nooria, A. Reproductive cancer risk factors among relatives of cancer patients seeking treatment in Hacettepe University Oncology Hospital. Hacettepe University Institute of Health Sciences, M.Sc Thesis in Cancer Epidemiology, Ankara, 2014. This study is an attempt to measure the frequency of specific gynecological cancer risk factors in female relatives of cancer patients**.** A cancer risk assessment questionnaire had been designed in the Department of Preventive Oncology, and filled by relatives of cancer patients admitted to Hacettepe University Oncology Hospital in order to be diagnosed and/or treated. The data were collected through the years 2007 to 2012. The mean age of the study population was 45.7±12.2 years. Median age at menarche was 13 years (IQR, 12-14), 6.9% of the women reported their menarche before age of 12. About 11.1% of the women had intercourse before age of 18. The median age at first delivery was 22 years. Median BMI was 24.9, with 18.3% of obesity. Of the women 65% were current/past smokers. Only 2.5% of women in this study reported at least one positive diagnosis of STDs in their lives. Sixty-two percent of the women had never used condom. About 8% of the women were unaware about mammography and 17.7% about the Pap test. Compared to general Turkish population, women participated in this study were more likely to be older. The prevalence of some reproductive cancer risk factors was consistent with estimates provided in the literature, but not all of them. Compared to the Pap test awareness and behavior of the women were better about mammography. Considering our results, some measures should be put in place to increase people's awareness, and to modify their behavior toward cancer screening tools. For cancer prevention, people's lifestyle modification is required. These findings indicate need for further and more generalized studies to measure cancer risk factors prevalence in general Turkish population.

Key words: Gynecologic Cancer, Risk assessment, Risk factor, Early detection of cancer, Cancer screening.

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ABBREVIATIONS

ADC	Adenocarcinoma
ASC	Adenosquamous carcinoma
BMI	Body mass index
BRCA1&2	Breast cancer gene mutations
CI	Confidence interval
CT	Computed tomography
CIN	Cervical intraepithelial neoplasia
DES	Diethylstilbestrol
E1	Estrone
E2	Estradiol
FRA-BOC	Familial Risk Assessment – Breast and Ovarian Cancer
HNPCC	Hereditary non-polyposis colorectal cancer
HPV	Human papilloma virus
HRT	Hormone replacement therapy
HSIL	high-grade squamous intraepithelial lesion
HSV	Herpes simplex virus
MRI	Magnetic resonance imaging
OCP	Oral contraceptive pills
OR	Odds ratio
RR	Relative risk
SCC	Squamous cell carcinoma
SERM	Selective estrogenic receptor modulators
SHBG	Sex Hormone-Binding Globulin

SIL	Squamous intraepithelial lesion
STD	Sexually transmitted disease
STI	Sexually transmitted Infections
TVUS	Trans-vaginal ultrasound
VLP	Virus like particle

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1. INTRODUCTION

Cancer is the uncontrolled growth and spread of cells. It is one of the leading causes of death worldwide, and was accounted for 8.2 million deaths in 2012 (1). Women's genital organs as other parts of the human body can be affected by cancer.

Overall etiology of gynecologic cancers is not well understood. However, some of causative factors are known for these cancers. However, women with and without risk factors may both develop gynecologic cancers. The distribution of risk factors for gynecologic cancers (as well as other cancers) is not same in all parts of the world. After identifying the risk factors, it is important to find out about their prevalence in a specific population in order to prevent and manage cancer.

In some of gynecologic cancers, by preventing causative agents, almost all cases of that cancer can be prevented, such as HPV infection prevention for cervical cancer (1). On the other hand, early detection of population under risk and its management in these populations will increase the chance of complete cure in endometrial and cervical cancers. Unfortunately, ovarian cancer denoted as "silent killer" among gynecologic cancers, because it is often diagnosed at an advanced stage when its cure is difficult. There are some known risk factors like hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome that can increase chances of ovarian as well as endometrial cancers.

Assessing cancer risk in average and high-risk people are essential for early detection and primary prevention of cancers in women. There are some risk assessment tools, for some cancers such as Familial Risk Assessment – Breast and Ovarian Cancer (FRA-BOC) (3) and Gail model (2).

In Turkey, to our knowledge, there has not been done a risk assessment study yet. To do risk assessment, defining the risk factors' prevalence in a particular population is vital. The aim of this study is to evaluate the prevalence of some reproductive cancer risk factors in a

population of female relatives of cancer patients seeking treatment in Hacettepe University Oncology Hospital.

2. REVIEW OF LITERATURE

Worldwide, there were 14.1 million new cases of cancer, 8.2 million cancer deaths and 32.6 million people living with cancer in 2012 (1). Fifty-seven percent (8 million) of new cancer cases, 65% (5.3 million) of cancer deaths and 48% (15.6 million) of 5-year prevalent cancer cases occurred in the less developed countries (1).

For men the overall age standardized cancer incidence rate is 25% higher than in women globally (205 vs. 165 per 100,000) (1). The incidence rate of cancer varies across the different regions. This variation for male is fivefold, while for female is almost threefold, with rates ranging from 103 per 100,000 in south-Central Asia to 295 per 100,000 in Northern America. The rate in Turkey is 173.3 per 100,000 (3). However, cancer-related deaths have lesser regional variations .

Gynecologic cancers primarily originate from uterine corpus, ovaries, uterine cervix, vulva and vaginal tissues.

2.1 Uterine Cancer

Cancers originating from uterine body cells are called uterine cancers. According their origination site, histological structure, and their treatment options, uterine cancers are divided to endometrial carcinoma and uterine sarcoma.

Endometrial cancer -about 95% of cases- originates from the endometrial mucosa. The most common histological type of uterine corpus tumors is adenocarcinoma. Uterine sarcoma is a rare type- less than 5% of uterine cancers - that forms in muscle or other connective tissues of the uterus. Uterine sarcomas usually occur after menopause and have two main types; leiomyosarcoma (cancer of smooth muscle cells) and endometrial stromal sarcoma (connective tissue cells of the endometrium).

According to WHO, the worldwide incidence of uterine cancer is 319,605 annually, which represents 4.8% of all cancers. The incidence rate of uterine cancer is 8.3 per 100,000 women worldwide (1). According to latest provided data in Turkey the incidence rate of uterine cancer is 9.3 per 100,000 women in a year (3) with an estimated mortality rate of 2.6 (3). The most common gynecologic cancer in the United States is uterine cancer (6% of all cancers in U.S women in 2013) (4). The incidence rate of endometrial cancer in the U.S.A is 24.3 per 100,000 women per year and has been increasing by an average of 1.1% per year since 2004. Approximately 2.7 percent of women will be diagnosed with endometrial cancer at some point during their lifetime. There are approximately 600,346 women currently living with endometrial cancer in the United States. 81.5% of them will survive for 5 years or more (4).

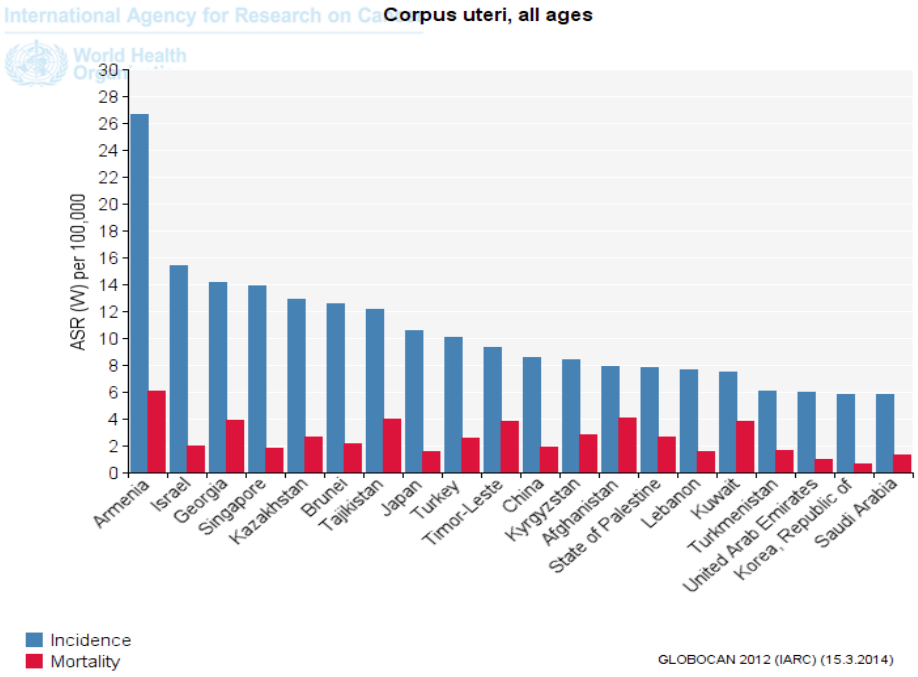


Figure 2.1. Incidence/ mortality of uterine cancers in Asia, including Turkey

2.1.1 Etiology and Risk Factors for Endometrial Cancer

The cause of uterine cancer has not been fully understood. The disease primarily affects postmenopausal women at an average age of 60 years at diagnosis. Some risk factors are described for the disease; including, exposure to long-term or high dose of estrogen; reproductive factors like nulliparity, no or lesser lactation; some disease/ syndromes such as polycystic ovarian syndrome and tamoxifen use. Women with Hereditary Nonpolyposis Colorectal Cancer (HNPCC) syndrome have a markedly increased risk (20-60%) of endometrial cancer compared with women in the general population (5,6). Table 2.1 shows risk factors for uterine cancers and their estimated relative risks.

Table 2.1. Factors influencing risk for uterine corpus cancer (7)

Factors Influencing Risk	Estimated Relative Risk*
Older age	2-3
Residency in North America or Northern Europe	3-18
Higher level of education of income	1.5-2
White race	2
Nulliparity	3
History of infertility	2-3
Menstrual irregularity	1.5
Late age at natural menopause	2-3
Early age at menarche	1.5-2
Long term use or high dosage of menopausal estrogen	10-20
Long term use of combined oral contraceptives	0.3-0.5
High cumulative doses of tamoxifen	3-7
Obesity	2-5
Stein-Leventhal disease or estrogen producing tumor	>5
History of diabetes, Hypertension, gallbladder disease, or thyroid disease	1.3-3
Cigarette smoking	0.5

*relative risk depend on the study and different group employed.

Age

Uterine cancer primarily affects postmenopausal women, with a median age at diagnosis of 60 years (4). The risk increases rapidly with age

during childbearing years. After menopause rates continue to increase, but at a less rapid manner (7).

Estrogenic Effects:

There is evidence that long-term exposure to estrogen and its metabolites increases risk of uterine cancer. Exposure to estrogen could be endogenous or exogenous.

Endogenous Estrogens:

- **Early Menarche and Late Menopause**

Early age at menarche (before age of 12) was found to be related to increased uterine cancer risk (8). Studies have indicated that the age at menopause (after age of 55) is directly related to the risk of developing uterine cancer. For these women, it is hypothesized that prolonged uterine exposure to estrogen stimulation in the presence of anovulation (progesterone-deficiency), reflects the increase in risk (7).

- **Parity and Lactation**

The evidence indicates the presence of an inverse association between the increase in parity and duration of lactation with the risk of endometrial cancer. Parous women have a decreased risk of endometrial cancer compared with nulliparous women. The evidence confirmed a reduction in risk of endometrial cancer in multiparous women. The explanation is a lower cumulative exposure to estrogen and/or higher exposure to progesterone. Serum level of Sex Hormone-Binding Globulin (SHBG) is lower in nulliparous women, as a result free estrogen level is higher in these women. An increasing number of full term pregnancies and shorter menstrual lifespan support an important role of hormonal mechanisms in endometrial carcinogenesis (9). On the other hand, there is no apparent importance of age at first childbirth. A last birth occurring late in reproductive life may reduce the risk. Possible reasons could be a unique

hormonal profile of the women who are able to conceive at older ages and mechanically clearing malignantly transformed cells from the uterine lining.

There are controversies about the role of breastfeeding and its duration in decreasing risk. In some studies a 23% risk reduction noted with breastfeeding more than 18 months. The risk reduction was attenuated when adjusted for parity (9,10).

- **Infertility**

Studies showed that infertile women have a 3 to 5 fold-increased risk of endometrial cancer compared to the general population (7). The increased risk is more than for nulliparous women without infertility. Here are several biological explanations for increasing risk in infertile women such menstrual cycles (prolonged exposure to estrogen without sufficient progesterone), high serum levels of androstenedione (for conversion to anovulatory estrogens such as; estrone) and absence of monthly sloughing of endometrium (may cause endometrial hyperplasia).

- **Obesity**

Obesity and being overweight are associated with an increased risk of endometrial cancer. The possible reason for this association could be an increased level of serum estrone (E1) in these women. Production of estrogen increases in adipose tissue as a result of aromatization of androstenedion. On the other hand, obesity decreases the levels of SHBG, thus increasing "free" estradiol (E2) available to target tissues. Obesity has been associated with several factors claimed to increase the risk of endometrial cancer including upper-body or central adiposity, polycystic ovarian syndrome, lower physical activity, and a diet high in saturated fat (11). The risk of endometrial cancer increases 1.59-fold per 5 kg/m^2 change in body mass (12).

Exogenous Estrogens:

- **Postmenopausal Hormone Therapy**

An association between estrogen replacement therapy and endometrial cancer was first reported in 1975 (15). Afterwards, it was confirmed that unopposed estrogen is associated with an increased risk of endometrial cancer. There is also an association between endometrial cancer and duration of estrogen use (10-fold to 30 fold increase with 5 years or more of use). Cessation of estrogen use leads to a relatively rapid decrease in the risk. But, a long lasting effect for more than 10 years after only 1 year's use has been documented (13). It is observed that all doses of estrogen can increase the risk, with some evidence of association between higher doses and increased risk (7). It seems that exogenous estrogen's effect and its metabolism in thin, non-diabetic, or normotensive women differ from obese, diabetic and hypertensive women (already high risk groups). In the latter women's groups exogenous estrogen has only a small additional effect on risk compared to the previous ones (7). The excess risk of endometrial cancer associated with postmenopausal unopposed estrogen therapy can be eliminated by adding progestin, but progestin increases risk of breast cancer (14). There was an increment in serious health problems such as cardiovascular disease, stroke, and pulmonary embolus after a mean of five year treatment with combined oral contraceptives (estrogen and progestin) (1,15).

- **Selective Estrogen Receptor Modulators (SERM): Tamoxifen and Raloxifene**

These agents have divergent estrogen agonist and antagonist effects in different target organs. Because of t estrogenic effects of tamoxifen on the endometrium, it can increase risk of endometrial cancer. There is evidence that the risk of endometrial cancer increases following tamoxifen therapy for invasive breast cancer (16). The National Surgical Adjuvant

Breast and Bowel Project, Breast Cancer Prevention Trial P-1 Study in women at high risk of invasive breast cancer demonstrated that tamoxifen decreased breast cancer incidence by 49%, but confirmed an increased incidence of endometrial cancer. The annual rate was 2.3 per 1000 for women receiving tamoxifen versus 0.91 for those on placebo. Women older than 50 years experienced the largest effect (17).

Raloxifene is a second-generation SERM approved for prophylaxis against postmenopausal osteoporosis. Unlike tamoxifen, it does not have an estrogenic effect on the uterus. Still, there is a need for providing further evidence to conform no association between risk of uterus cancer and this agent. The Multiple Outcomes of raloxifene randomized trial, after 40 months of follow-up, showed that raloxifene reduced the risk of estrogen receptor–positive breast cancer, without increasing endometrial cancer (RR = 0.8; 95% CI, 0.2–2.7) (18). A population-based study of 547 women with endometrial cancer and 1,410 controls was done. The odds of endometrial cancer among raloxifene users was 50% that of non-users (odds ratio [OR] = 0.50; 95% CI, 0.29 to 0.85), whereas tamoxifen users had three times the odds of developing endometrial cancer compared with raloxifene users (OR = 3.0; 95% CI, 1.3 to 6.9) (19).

Familial and Genetic Factors

Familial history is suggested to be a risk factor for uterine cancer. Women with familial history of colon cancer are at increased risk, which reflects the role of the dominantly inherited Hereditary Nonpolyposis Colorectal Cancer (HNPCC) gene. Among women who are HNPCC gene carriers, the estimated cumulative incidence of endometrial cancer ranges from 20% to 60% by age 70 years (5,6). This risk appears to differ slightly based on the germ-line mutations; for MLH1carriers the lifetime risk at age 70 years is 25% while, MSH2 mutation carriers have a 35% to 40% lifetime risk of endometrial cancer by age 70 years. The mean age of diagnosis

for MLH1 or MSH2 carriers is 47 years compared with 60 years for non-inherited forms of endometrial cancer (20).

Some Medical Predispositions

A variety of diseases have been suggested as possibly predisposing to uterine cancer risk. But there are some controversies, because the effect of the risk was attenuated when adjusted for obesity (concomitant with almost all of those diseases). Polycystic ovary syndrome with a feature of hyperandrogenism and chronic anovulation can increase the risk (21).

Diabetes is another medical condition supposed to increase the risk of endometrial cancer. Metabolic abnormalities including hyperinsulinemia could be the possible explanation.

Hypertension, thyroid and gallbladder diseases, and hypercholesterolemia are the diseases of observed relationships with uterine cancer risk. But, still no strong evidences are provided for these relationships. Further studies are needed to define independent association of all above medical conditions with the risk of uterine cancer (7).

Geographical Place of Residence

The incidence rate of uterine cancer varies geographically. Data from well-run registries around the world (age-adjusted, world standard) show variations in incidence rate from lowest in parts of China, Japan, India to highest in white women from the United States (7). Besides, an apparent within country variation in rates of the disease was observed. Rates in urban areas generally exceeded those in neighboring rural areas.

Demographic factors that might account for the variation include upper socioeconomic status lifestyle, diet, over nutrition, and estrogen replacement therapy. Besides, reproductive behavior can also play a role in the risk. In addition, compared to whites the incidence rate are lower among black women in the United States. Still there is no clear explanation for that

difference in rates, may be related to reproductive behavior, socioeconomic status, and access to medical care (early diagnosis and effective treatment in white population) (7).

2.1.2 Risk Factors for Uterine Sarcoma

Etiologic factor is only documented in 10% to 25% of uterine sarcomas. These include prior pelvic radiation therapy which is often administered for benign uterine bleedings. In most of these cases, uterine sarcoma is diagnosed about 5 to 25 years later to radiation therapy. An increased incidence of uterine sarcoma has been associated with tamoxifen in the treatment of breast cancer—a possible result of the estrogenic effect of tamoxifen on the uterus (2).

2.1.3 Clinical Synopsis of Uterine Cancer

Postmenopausal bleeding is the most common symptom of uterine cancers and occurs in 90% of cases. Premenopausal patients with uterine cancer admit to hospital irregular and/or heavy menstrual bleeding. In patients with symptoms, transvaginal ultrasound (TVUS) and endometrial sampling are first diagnostic steps. In a suspected patient, endometrial biopsy is usually performed. If the biopsy is negative, then a dilatation and curettage is completed to get a better sample. However, there is no routine population based screening tool for uterine cancers (2). For diagnosis and determination of extent of the disease, diagnostic procedures such as cystoscopy, proctoscopy, computed tomography (CT) and magnetic resonance imaging (MRI) could accordingly be done (21). Treatment decisions for uterine cancers depend on lesion severity, patient’s age, medical history, and the patient’s preference.

Treatment options in patients with uterine cancer include surgery, radiation therapy, endocrine therapy and chemotherapy. Early stage endometrial cancer is curable and requires hysterectomy and bilateral salpingo-oophorectomy. Best results are obtained with either of two standard treatments: hysterectomy alone or hysterectomy followed by adjuvant radiation therapy. Most patients with stage I treat with surgery alone. A subset of patients with stage I disease are at a high risk of recurrence and are eligible for adjuvant cytostatic therapy (22). Stage II patients and those in more progressed stages would get individualized combinations of pelvic and external irradiation and subsequent surgery; and patients with the most advanced disease would receive cytotoxic drugs or endocrine therapy (palliative). The 5-year survival rate is 70% to 80% in the developed world, ranging from 90% for stage I patients to 20% for stage IV (22). Sarcomas also can be treated with surgery, radiotherapy and/or chemotherapy according the stage and depth of the lesion.

2.1.4 Prevention of Uterine Cancer

Some interventions and lifestyle modifications - avoiding exposure to modifiable risk factors as much as possible can lower the chance of developing uterine cancers. Timely and proper medical treatment for precursor disorders (e.g. endometrial hyperplasia) of the disease is advised. Long term hormone therapy decreases the risk. Caution is also recommended with the use of phytoestrogens, because their long term safety is unknown (24). Appropriate diet and exercise are important to decrease the risk.

2.2 Ovarian Cancer

Malignant ovarian neoplasms causing more deaths than any other female genital tract cancers are named as "silent killer" in women, because the majority of the cases are already at advanced stages by the time of diagnosis (21). They can occur at all ages including infancy and childhood.

The majority of the cases (85-95% in U.S.A) are epithelial ovarian cancers. Epithelial ovarian cancers are seen primarily in women over 50 years. Non-epithelial ovarian cancers are usually originated germ cell and they are classified as embryonal endodermal sinus, yolk-sac tumor, dysgerminoma and teratoma. They are seen more often in young women or adolescent girls. These tumors are frequently unilateral and aggressive. However, they are generally curable if found and treated early. Most rare tumors are derived from follicular cells are sex-cord stromal tumors (most often granulosa cell tumors) and sarcomas risen from stromal elements of the ovary (7).

According to the GLOBOCAN, 2012 an estimated 238,719 new cases of ovarian cancers are diagnosed annually all over the world, which represents 3.6% of all cancer cases. The crude incidence rate of ovarian cancer is 6.8 per 100,000 while, its age standardized incidence rate is 6.1 per 100,000 women in year (1). Internationally its estimated age standardized mortality rate is 3.7 per 100,000 with a number of estimated 151,905 deaths per year. It is estimated that 56.6% of deaths will occur in less developed countries (1). White women have higher incidence and mortality rates than women of other racial/ethnic groups (2) . In Turkey the incidence rate of ovarian cancer is 6.9 per 100,000 women per year with an estimated number of 1,600 (1). The mortality rate for ovarian cancer in Turkey is 4.2 (a number of estimated1588 people). Figure 2.2. shows 20 Asian countries with the highest ovarian cancer rate.

In the United States the incidence is 11.8 per 100,000 per year, with an mortality rate of 9.6 (21). There are an estimated 186,138 women currently living with ovarian cancer in the United States. Of which only 44.2% is estimated to survive 5 years or more after being diagnosed (4).

Approximately 1.4 percent of women will be diagnosed with ovarian cancer at some point during their lifetime (2).

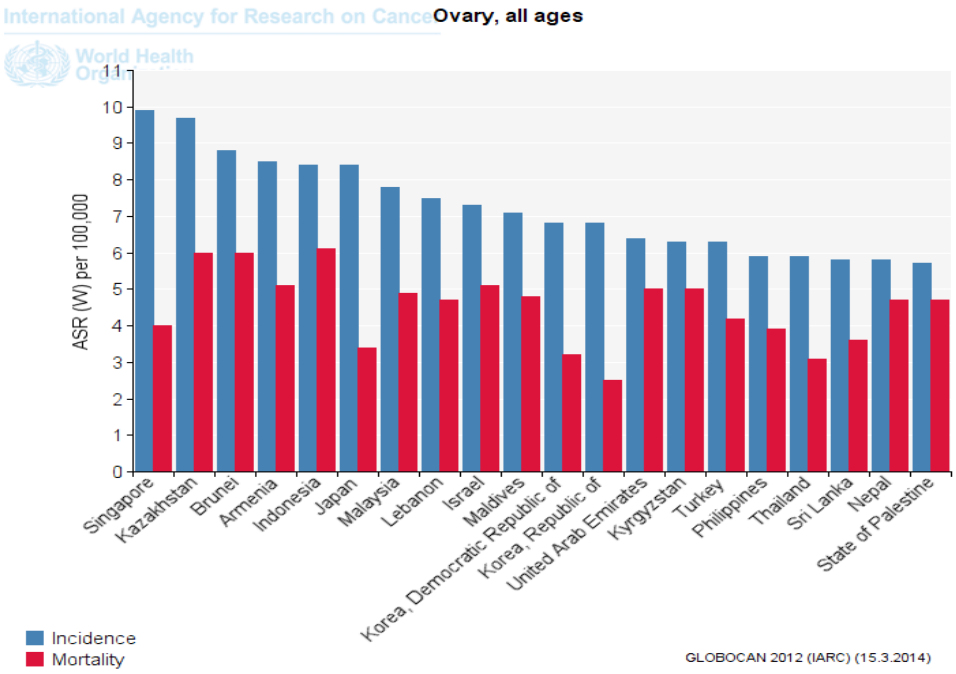


Figure 2. 2. Twenty Asian countries with the highest ovarian cancer rates

2.2.1 Etiology and Risk Factors of Ovarian Cancer

The etiology of ovarian cancer is still unclear and mostly unpredictable. Two main theories about its etiology are: “the incessant ovulation hypothesis” and “the gonadotropin hypothesis”. Both of them are based on the increasing number of ovulation- repeated cell division, increasing the possibility for replication error, ineffective DNA repair, and subsequent ovarian epithelial cancer. In another theory, chronic inflammation is a contributing factor in the presence of the cancer, e.g. inflammation caused by talc products or asbestos exposure, but not confirmed (21). There are some known factors appear to modify the risk of ovarian cancers:

Family History of Cancer and Genetic Factors

Approximately 5% to 10% of ovarian cancers, especially in younger age are familial. Three distinct hereditary patterns have been identified; ovarian cancer alone, ovarian - breast cancers, and ovarian - colon cancers (23).

The most important risk factor for ovarian cancer is a family history of a first-degree relative (e.g. mother, daughter, or sister). The highest risk appears in women with two or more first-degree relatives having ovarian cancer. A woman with a single family member with ovarian cancer has a 4-5% risk of developing ovarian cancer, compared to the lifetime risk of 1.6% for the general population. The risk increases to 7% for those with two relatives with ovarian cancer. The risk is somewhat less for women with one first-degree and one second-degree relative (grandmother or aunt) with ovarian cancer (24,25).

In most families with the breast and ovarian cancer syndrome, involvement of germ-line mutations in BRCA1 (chromosome 17q21) and BRCA2 (chromosome 13q12) has been found. The lifetime risk for ovarian cancer as well as breast cancer in these mutations carriers are significantly higher than the general population (26). Comparing BRCA1 mutation to BRCA2, it has been found that risk of ovarian cancer in the former is higher than the latter. Disease onset is earlier in these patients and multiple cancers in some of BRCA1 mutation carriers could be found. The lifetime risk of ovarian cancer in presence of BRCA1 and BRCA2 mutations is 10-40% (27). BRCA1 gene mutation carriers also have a high risk of fallopian tube carcinoma (RR, 45) (28).

Another most common familial hereditary abnormality for ovarian cancer is Hereditary Nonpolyposis Colorectal Cancer (HNPCC) syndrome (Lynch syndrome). The lifetime risk of ovarian cancer with Lynch syndrome is 4-12% (29). Beside early onset of ovarian cancer, there are more cases of synchronous endometrial cancer reported in these patients (21). Mutations in hMSH2 and hMLH1 genes is presented in Lynch syndrome

which are consistent with an increase in both gynecological and gastrointestinal malignancies.

Nulliparity

There are data from both case-control and prospective cohort studies that show a protective effect of parity on ovarian cancer risk. In accordance with ovulation theory, pregnancy prevents ovarian cancer though inhibiting repeated ovulation. Pregnancy may exert long lasting effects on gonadotropines too. On the other side, higher levels of progesterone during pregnancy may have a role in decreasing the risk of ovarian cancers. So, nulliparity independently can be a risk factor for ovarian cancer. Each additional pregnancy associates with a 13% to 19% risk reduction. According available data failed pregnancies (miscarriages, abortions, ectopic pregnancy) would confer less protection.

Infertility drugs

Women with fertility problems differ from those without such problems in terms of other established ovarian cancer risk modifiers, such as parity or oral contraceptives. The issue is further complicated by the need to separate the biologic effects of infertility itself from the effects of the medications used to treat this problem. Clomiphene citrate and human chorionic gonadotropin are used to induce ovulation in infertile women. In varying degrees all these agents increase the number of ovulations per cycle, number of follicles and the number of oocytes. On the other hand, there is the possibility of increasing level of estrogen and progesterone in these women. Results obtained from some case-control and cohort studies showed that ovulation induction increased the risk of ovarian cancer, especially in case of prolonged use of the medications (30). However, some other studies showed no increase in risk. A meta-analysis of eight case control studies found that drugs used for fertility in nulligravid women associated with increased risk of borderline malignancies, no increase in risk of invasive ovarian cancers. Among those who were nulliparous but

who had been pregnant, these drugs was not associated with increased risk (30).

Age; Age at Menarche and Menopause

Ovarian cancer can occur in all age groups, even in infants. About 85% of all ovarian cancers are epithelial carcinoma, with 50% of all cases occurring in women older than 60 years. Moreover, in older women, ovarian cancer is more likely to diagnose in advanced stages. So, mortality in women of 65 years and older is higher than younger women (31). There is a strong association between age and incidence and mortality of ovarian cancers. However, there is a weak association between ovarian cancer and early age at menarche (before age of 12).

For age at menopause, there is no significant evidence of association between ovarian cancer and “natural” (i.e. non-surgical) age at menopause. Although a few case control studies found a modest positive association between them (30).

Postmenopausal Hormone Therapy

Postmenopausal hormone therapy (PHT) is associated with a significant increase in risk of ovarian cancer. A cohort study of women who participated in the Breast Cancer Detection Demonstration Project showed an increasing effect of PHT on ovarian cancer risk, with RR of 1.6 (95% CI, 1.2 –2.0). Also the risk associates with duration of hormontherapy, as those who took estrogen for 20 or more years had more than three times greater risk than that of never-users (RR, 3.2) (32). An association between postmenopausal estrogen use and ovarian cancer mortality also has been shown. Data suggests that women with short-term PHT or a combination of estrogen-progestin may be safer. Still, there is a need for further evidence, especially about long-term use of combined hormone therapy (30).

Talc Exposure

An increasing effect of perineal talc use on ovarian cancer risk was suggested by some case control studies. A metaanalysis including case control studies found a modest increase in ovarian cancer incidence among women who reported exposure to talc (adjusted RR, 1.3; 95% CI, 1.1 to 1.5) (30). However, there was no evidence of a dose-response effect. A cohort study among nurses did not observe an increase in risk of ovarian cancer with perineal talc use (RR = 1.09; 95% CI, 0.86–1.37) (33). The suggested possible mechanism for this association is chronic inflammation due to talc as well as asbestos exposure.

2.2.2 Clinical Synopsis of Ovarian Cancer

Typically the disease in early stages is asymptomatic, even in advance stages, symptoms may be non-specific. These symptoms are usually gain weight, abdominal/pelvic discomfort, early satiety, changes in bowel habits, irregular vaginal bleeding. By examination, an adnexal mass (irregular and mostly solid) can be found. Trans-vaginal ultrasound and blood concentration of CA-125 as well as test of liver and renal functions can be done at the next step. Further evaluations can be done by abdominal ultrasound, chest X-ray, CT, and MRI as needed.

Ovarian cancers in early stage (IA) can be treated by surgery, chemotherapy and/or radiation. Debulking surgery should be perform in advanced setting. Chemotherapy is corner-stone in advanced stage, but in more than 75% cases, the disease can relapse within the first 2 years (21).

In order to improve overall survival, adjuvant chemotherapy is used. Neoadjuvant chemotherapy is advised in stage III disease and /or in patients who have no suitable for surgery in time of the diagnosis. In recurrent disease, chemotherapy is the first choice for treatment. Radiation has no impact on overall survival in early stage disease. Radiation can be

used for palliation of symptoms in patients with recurrent pelvic disease and/or bowel obstruction (21).

2.2.3 Screening and Prevention of Ovarian Cancer

Ovarian cancer does not have a known pre-malignant process/lesion. So, it is difficult to screen population for early detection. However, in women with a positive family history and confirmed genetic risk factors, the National Institute of Health recommends annually monitoring by pelvic examination, and CA-125 concentration testing. Also trans-vaginal ultrasonography every 6 months is recommended (21).

Factors associated with a decreased risk of ovarian cancer are:

1. Using oral contraceptives
2. Having and breastfeeding children
3. Having a bilateral tubal ligation or hysterectomy
4. Having a prophylactic oophorectomy.

There is a significant evidence that use of combined oral contraceptive (OCP) is consistent with a decrease in ovarian cancer risk in the general population. The risk in OCP users is 30% lesser than non-users and the risk continues to decrease about 5% each year (21). A review of the literature demonstrated a 10% to 12% decrease in risk associated with OCP use for 1 year and an approximately 50% decrease after 5 years of use. This reduced risk was presented among both nulliparous and parous women (34). In subjects with a familial history of ovarian and breast cancer, the use of OCP should be look over because of increased risk (35).

Data show that parity has a protective effect on ovarian cancer risk even in BRCA1 or BRCA2 mutation carriers (36).

A significant inverse association between ovarian cancer and tubal ligation has been found. The risk is lower about 33% in women with tubal ligation compared to the general population (35). Also, mortality from ovarian cancer decreases (30). The biological mechanism of this

association is unclear; possibly decreased access of environmental carcinogens, or changes in blood flow of the ovaries.

Prophylactic oophorectomy after completion of childbearing (mostly after age 35) may reduce the risk of developing ovarian cancer for women at high risk (familial or genetic risk). Again risks (early menopause, potential morbidity and mortality of surgery, etc.) of oophorectomy versus its benefits should be taken into account when considering prophylactic oophorectomy (21).

2.3 Cervical Cancer

Cervical cancer is the second most common cancer in women worldwide, while the least common among gynecological cancers in the United States. The main reason of declining in incidence and mortality from cervical cancer in the last 50 years is its early detection (attributed to Pap smear screening program), and applying preventive measures to the general population. Because of limited availability of advanced screening techniques in developing countries, more than 85% of cervical cancer cases occur there. This cancer is a slow growing cancer and almost all cases are caused by the Human Papilloma Virus (HPV) infection (2). The worldwide incidence of cervical cancer is 527,624 which represents 7.9% of all cancer cases. According to GLOBOCAN, 2012 the incidence rate of cervical cancer is 14 per 100,000 women per year worldwide (1). Every year, more than 270, 000 women die from cervical cancer; more than 85% of these deaths are in low- and middle-income countries (4). The highest incidence and death rates are reported in Latin America and Caribbean, Sub Saharan Africa, South and Southeast Asia. Whereas, low rates are in most developed countries, China and western Asia (Figure 2. 3). The incidence rate of cervical cancer in Turkey is 4.5 per 100,000 per year, and 1.7 is its mortality rate (3).

Cervical cancer generally affects multiparous women at early postmenopausal years. Of cervical cancers, 75-80% are squamous cell

carcinoma (SCC). Adenocarcinoma and adenosquamous carcinoma (ASC) account for 10-15% of cases. Cervical cancer is preceded by inter epithelial changes called cervical intraepithelial neoplasia (CIN), based on the histologic appearance. The alternative of CIN in terms of cytopathologic diagnosis is squamous intraepithelial lesion (SIL). This precancerous phase occurs over a long period of 10 -20 years and can be detected by cytological examinations. Cervical cancer is rare in women under 30 years and is more commonly diagnosed in ages after 40, with greatest mortality is in ages of 50s and 60s.

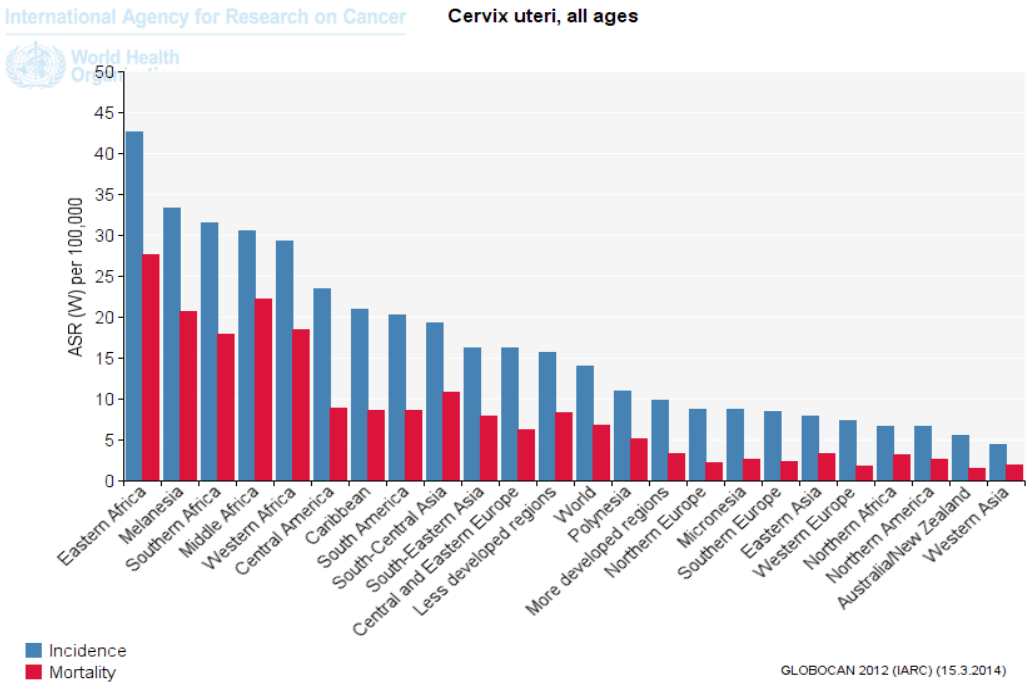


Figure 2. 3. Worldwide incidence/ mortality rates of cervical cancer

2.3.1 Etiology and Risk Factors of Cervical Cancer

Evidence showed that human papilloma virus (HPV) infection is a central etiologic factor in almost all cases of cervical cancer (36). As HPV infection is a sexually transmitted disease (STD), cervical cancer is seen mostly in sexually active women at high risk of STDs such as women with multiple sexual partners (each additional partner adds another 25% to the

risk of HPV exposure) (21), unprotected sexual activity, early ages in starting sexual activity and reproductive life. HPV infection has a bimodal age distribution with a peak at younger ages (<25 years), declining to a plateau in middle age, and a modest second peak ⩾ 45 of age (37). Therefore, cervical cancer is seen more frequently in women having early sexual activity history with multiple partners.

Approximately 100 distinct types of HPV have been defined by now, more than 30 of which infect human genital tract. About 14 types of HPV are associated with cervical cancer. HPV DNA is detected in more than 90% of cervical cancer (range from 75% to 100%) (38) , in up to 94% of women with pre-invasive lesions (cervical SIL), and in up to 46% of women with cytologically normal findings (39). The most common types of HPV linked to cervical cancer are types 16 and 18 (responsible for about 70% of cases). While HPV 16 is the most common type, HPV18 is more common in aggressive cases (40). The risk of cervical cancer in HPV positive women has been reported to range from 16 fold to 122 fold (39).

Despite the causal link of HPV infection with cervical cancer, only a small proportion of HPV infections progress to pre-cancer or cancer. Almost 80% of newly diagnosed infections clear within 12 to 18 months. Findings suggest that HPV infection has a central role in cervical neoplasia occurrence, but is not sufficient by itself, and may need other environmental, viral, and host-related cofactors to do so. It is suggested that these co-factors have no independent effect on cervical cancer risk, instead may influence the acquisition of HPV infection, increase likelihood of persistent HPV infection (most critical in cervical carcinogenesis), or increase risk of progression from HPV infection to high-grade squamous intraepithelial lesion (HSIL). Reports from epidemiologic studies indicate higher sero-reactivity to E6, E7 and virus like particles (VLPs) among patients with cervical cancer. Antibody against HPV-16 was found in most women without cervical lesion, but not in those with active disease. In addition to viral type, concurrent multiple infections, intra-typical variation of

HPVs and high viral load have been suggested as risk factors for persistent infection and progression to neoplasia.

Parity as a Cofactor

Among HPV-infected women, those who have had seven or more full-term pregnancies have increased approximately four times the risk of cervical SCC compared with nulliparous women, and two to three times the risk of women who have had one or two full-term pregnancies. In addition, early age at first pregnancy is strongly associated with increased the risk. About 4.4 fold higher risk has been found in women with first full term pregnancy before age 17 (41). Repeated trauma of the cervix and hormonal, immunological, and nutritional factors are suggested as possible mechanisms of the increase in the risk. In an analysis (not restricted to HPV-positive) women with a history of seven or more full-term pregnancies were at 1.6 folded increase risk of cervical cancer compared to nulliparous women (39).

Oral Contraceptives (OC) as a Cofactor

There are some controversies on the association of hormonal contraceptives and risk of cervical cancer. Most epidemiological studies have found a positive association of long term OC use and risk of cervical cancer after controlling for HPV and other confounders. Based on evidence obtained from cohort and case-control studies, long-term use of oral contraceptives is associated with increased risk of cervical cancer. Studies of HPV-infected women have shown that those who had used OCs for 5 to 9 years have an approximately three-fold higher incidence of invasive cervical cancer, and those who used OC for 10 years or longer have approximately four times the risk than never users. The increase in risk of less than five years use, was not significant (39, 42).

Two possible mechanisms have been proposed; first, increased exposure of the transformation zone to carcinogens (increased incidence of

cervical ectropion among OC users would possibly increase the exposure of transformation zone to HPV and other carcinogens). But, there is no strong evidence to prove it. And second, increased cell proliferation by estrogen and progesterone, consequently, increase in HPV transcription, which has been supported. Steroid hormones increase exposure of HPV's E6/E7 oncogenes, promoting degradation of TP53, and involving in 16α-hydroxiestrone binding to estrogen receptors and prolonging its proliferative effects (39).

Smoking as a Cofactor:

Cigarette smoking, both active and passive smoking, is associated with the increased risk of cervical cancer. Among HPV-infected women, current and former smokers have approximately two- to three-times the incidence of high-grade cervical intraepithelial neoplasia (HSIL) or invasive cancer. Passive smoking is also associated with increased risk, but to a lesser extent (2). There is an association between risk of cervical cancer and amount and years of smoking. There is no significant (consistent) evidence about the independent effect of smoking on cervical cancer after controlling for HPV infection. High levels of nicotine, cotinine and tobacco special N-nitrosamine have been reported in cervical mucus of active and passive smokers. In addition, DNA damage in cervical tissue and impairment of the local cell mediated immune response has been documented in smokers. So, mechanisms for increasing risk of cervical cancer by smoking could be: as a direct carcinogen, or indirectly by disturbing host's local immune response which can assist HPV infection, its persistence and progression to cervical cancer.

Other Sexually Transmitted Diseases (STDs) as Cofactors

STDs is one of the co-factors in cervical carcinogenesis. HSV-2 and Clamidia.trachomatis play a role as cofactors in HPV-related carcinogenesis. But understanding of that role is limited by difficulties in investigating the biologic mechanisms involved. STDs may have a direct genotoxic effect or an indirect effect through inflammation. HSV-2 and C.trachomatis are associated with cervicitis (inflammation), which can lead to ectropion (when the central columnar epithelium extends out through and around the external os), facilitating HPV infection and its persistence. Some studies showed about two fold increased risk of HPV related cervical cancer in HSV-2 and Clamidia trachomatis positive women (39). But, an inconsistency in these study results has been found.

The frequency of cervical abnormalities (larger lesions, higher grades, and higher recurrence rate) is higher in HIV positive women compared to HIV negative women. HIV positive women have been reported to have higher rates of HPV infection (40% to 95%) and CIN lesions (10% to 36%) than HIV negative women (23% to 55% and 1% to 12% respectively) (39,43). As a result, it has been concluded that HIV is a cofactor for HPV related cervical carcinogenesis, and this association seems to be inversely related with the level of immune function (risk increases if CD-4 lymphocytes less than 500/mm^3) (39).

2.3.2 Screening of Cervical Cancer

Screening aims to detect precancerous changes which may lead to cancer. Adaptation of cervical cancer screening guidelines and adherence with it have been associated with a dramatic decrease in the incidence and mortality due to cervical cancer. American Congress of Obstetrics and Gynecology Screening Guidelines recommends routine screening including Papanicolaou test (Pap smear) and pelvic examination, which begins 3

years after the onset of vaginal intercourse annually before age 21. In women between 21 and 30 years old with three or more consecutive annual normal examinations, the Pap test may be performed once every 2 years. But in women with one or more risk factors should continue screening (Pap smear and pelvic examination) annually. After age 30, HPV test should be done once and repeated after abnormal Pap test finding. After the age of 30, the Pap test is advised once every 5 years up to the age of 65.

For women with multiple sexual partners, HPV test is advised annually. The serologic test for HPV is quantitative for viral load but can't distinguish between past and current HPV infection. In the next step, type of specific HPV DNA tests for high risk for HPV would be done. In women infected with high risk HPV, Pap smear should be done every 6 months. In case of abnormal Pap test with early signs such as atypical cells or mild dysplasia, follow up with Pap test every 6 months is advised. In case of higher- grade lesions colposcopy examination with endocervical curettage and biopsy should be done for final diagnosis (21). Regular screening, however, is associated with false positive test results (increase anxiety), large numbers of diagnostic procedures to evaluate abnormal tests, and treatment of low-grade lesions may adversely affect subsequent fertility and pregnancy (2).

Visual inspection with acetic acid (VIA) is an attractive alternative to cytology-based screening in low-resource settings. Similarly, cryotherapy has been selected as the treatment option for the eligible test-positive cases. The alternative cervical cancer-prevention techniques simplify the process and render it feasible and acceptable to women and providers in low-resource settings (1).

2.3.3 Clinical Synopsis of Cervical Cancer

In case of adherence to screening, most cases of cervical cancer are detected in precancerous stage, mostly asymptomatic. In case of established cancer cases, clinical feature can be; abnormal Pap test, abnormal vaginal bleeding, post coital bleeding, dyspareunia, difficult bowel movements, hematuria, urinary frequency, flank pain, etc.

Diagnosis is done with Pap test, colposcopy examination and confirmed in biopsy samples. Other diagnostic procedures may be needed accordingly.

Early stage cervical cancer can be totally cured with surgery. In such cases complete excision of tumor with negative margins is the goal of surgery. If needed a hysterectomy (total of radical) with affected lymph node dissection can be done. In recurrent and metastatic cases usually the aims of treatment are to palliate the symptoms, and control tumor growth and progression. In advanced cases radiotherapy is most often used in combination with chemotherapy. Radiotherapy can be external beam and then internal radiation.

2.3.4 Prevention of Cervical Cancer

Cervical cancer is almost completely preventable. By preventing HPV infection, cervical cancer can be prevented. And for HPV infection of the uterine cervix, sexual activity is critical. One can prevent cervical cancer by avoiding sexual activity throughout her life; however, this is unrealistic. Monogamy and condom use may decrease the risk of HPV exposure. Besides, on WHO guidelines, cervical cancer prevention can be summarized in three steps; primary, secondary, and tertiary prevention (1). Figure 2.4 shows WHO guidance note of comprehensive cervical cancer prevention and control: a healthier future for girls and women (1).

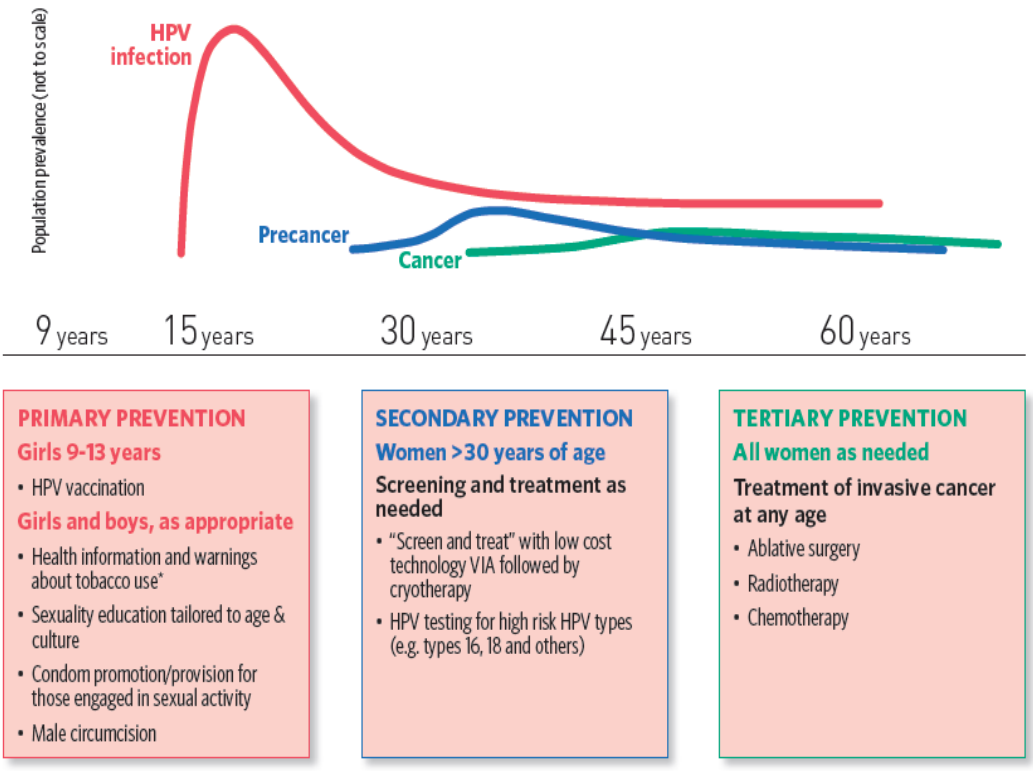


Figure 2.4. Overview of programmatic interventions over the life course to prevent HPV infection and cervical cancer

2.4 Vaginal Cancer

Vaginal cancers originate from vaginal cell and have two types; squamous cell carcinoma (85%) and adenocarcinoma. Vaginal cancer is one of rare forming 1% to 2% of gynecologic cancers. In the United States it was estimated to be 2,890 new cases of vaginal cancers in 2013. And this cancer is estimated to be responsible for 840 deaths in the United State during the year 2013 (2). In Turkey age adjusted incidence rate of vaginal cancer in 0.1 per 100,000 (3).

2.4.1 Etiology and Risk Factors

There is no known etiologic factor specific for vaginal cancers. Some risk factors have been suggested to increase the risk of vaginal cancer:

HPV Infection

HPV infection has been described as an important risk factor for vaginal cancers specially SCCs (2, 44).

Maternal Use of Diethylstilbestrol

Increased risk of clear cell adenocarcinoma of vulva, vagina and cervix as well as of breast cancer has been found in daughters (mostly in younger ages <30) of women who took dietilstilbestrole during pregnancy. Still, it is very rare; only 1 in 1000 daughters at risk (2).

2.5 Vulvar Cancer:

Same as vaginal cancer, vulvar cancer is rare. In Turkey its estimated incidence rate is 0.5 per 100,000 women per year (3). Approximately 0.3 percent of women will be diagnosed with vulvar cancer at some point during their lifetime (1). In United States, 4,700 new cases was estimated in 2013. Deaths due to vulvar cancer in the United States were estimated 990 for year 2013 (2). The average age of presentation is mid sixties for SCCs (90% of all vulvar cancers) but appears to have a bimodal age distribution with HPV mediated (basaloid and warty types).

No known etiologic factors. There are some risk factors for vulvar cancers, including infection (e.g. HPV), environmental/ industrial toxins, and chronic irritants. The basaloid and warty subtypes share many common risk factors with cervical cancers, including the multiplicity of sex partners, early age at initiation of sexual intercourse, and history of abnormal Pap smears. However, in 70-100% of them HPV infection has a central role (45).

There is no specific screening tools for both vaginal and vulvar cancers. Treatment protocols for vulvovaginal cancers include, surgery and/or radiotherapy according stage of the disease.

3. MATERIALS AND METHODS

This is a cross-sectional study, which has been done on available risk assessment data in Hacettepe University Cancer Institute's Preventive Oncology Department.

Data of 595 women was available in the Department's database; all of them have been included in this study. A cancer risk assessment questionnaire had been designed by the Department of Preventive Oncology and filled by relatives of cancer patients who admits to the Hacettepe University Oncology Hospital in order to be diagnosed and/or treated. Answering to the questionnaire was voluntary. The data were collected through the years 2007 to 2012. The questionnaire was completely self-administrated.

In our study, we primarily measured frequencies of specific risk factors for gynecologic cancers. In addition, level of women's awareness of available screening tools and their attitude/behavior toward them has been descriptively measured.

All variables were categorized into demographics, personal reproductive, personal/familial medical and drug history, and behavior/awareness categories for analysis. A summary of the measured parameters is presented here:

<u>Demographics</u>

- Age
- Residence
- Marital status
- Education
- Employment
- Insurance
- Monthly income

<u>Personal reproductive characteristics</u>

- Menarche age
- Menstruation

• Pregnancy
• Delivery
• Breast feeding
• Age at first intercourse

Personal/familial medical and drug history

• BMI
• Family history of cancer
• Chronic diseases
• Cancer history
• Regularly taken drugs
• Hormone replacement therapy, tamoxifen therapy, OCP taking
• Breast biopsy, mastectomy, and oophorectomy
• Sexually Transmitted Decease (STD) status in herself/sexual partner

Behavior/ Awareness

• Smoking
• Sport habits
• Diet, Alcohol
• Condom use
• Number of sex partner/s
• Condom use
• H/O Pap test
• Mammography
• Condom use

SPSS 20.0 package was used for data analysis. To analyze data firstly descriptive statistical methods have been applied. Mean ± standard deviation or median (IQR) has been calculated and used for representation of the quantitative data considering their distribution types. For categorical data frequencies were calculated. For comparison between groups of data specific methods such as chi-square test and t-test has been chosen and applied according the data type and distribution, number of groups and their dependency. To compare groups of data; for normal distributed two independent groups, such as; for age of all women, the independent

samples t-test was conducted and ANOVA in case of more than two groups. For not normally distributed data Mann-Whitney U or Kruskall-Wallis tests were conducted. Chi-square and Fisher's tests were used to determine the association between categorical data. To test the significance of the pairwise differences Bonferroni correction was used to adjust for multiple comparisons. The significance level was set at $p<0.05$. This study was approved by the Hacettepe University Ethical Committee (decision # GO 14/ 04 – 06).

4. RESULTS

This study included a total of 595 women with a mean (SD) age of 45.7 (12.2) years (ranged from 15 to 86) at the time of replying to the questionnaire (Table 4.1). The majority (68%) of the women was currently married and 10.7% of them were widowed or divorced, while only 21.3% of them had never been married yet.

Table 4.1. Summary descriptive values for demographic variables

Variable (valid data)	Group	Mean (SD)	N (%)
Age, yrs. (N=509) Mean ± SD (45.7± 12.2)	≤ 35	29.4 (4.4)	121 (23.8)
	36-55	46.2 (5.7)	276 (54.2)
	≥ 56	62 (5.2)	112 (22)
Residence type (N=107)			
	Urban		97 (90.7)
	Rural		10 (9.3)
Marital status (N= 558)			
	Married		379 (67.9)
	Single		119 (21.3)
	Divorced		37 (6.6)
	Widow		23 (4.1)
Education (N=570)			
	≤ Intermediate		240 (35.7)
	High school		185 (32.5)
	≥ University		181 (31.8)
Employment situation (N=542)			
	Housewife		240 (44.3)
	Officer		119 (22)
	Retired		77 (14.2)
	Worker		38 (7)
	Unemployed		26 (4.8)
	Student		24 (4.4)
	Business women		18 (3.3)
Monthly income (N=535)			
	≤ 500 TL		36 (6.7)
	500-1000 TL		175 (32.7)
	1000-3000 TL		270 (50.5)
	≥ 3000 TL		54 (10.1)

More than half (64.3%) of participants had completed high school and/or more, and only 175 (32.3%) of the women were currently employed (officer, worker, and business women). Half (50%) of the women reported their monthly income 1000- 3000 TL, while only 10.1% of them had an income more than 3000 TL/ month. All of the women who answered the question about health insurance had a health insurance, only 27 (4.5%) of women did not answer to this question. Most of the women replied to a question related to their residency, mentioned their living in cities (Table 4.1).

Median menarche age of the women in this study was 13 (IQR, 12-14) ranging from 10 to 20. The majority (84.1%) of the women reported their age at menarche to be between 12 and 15 years (including 15). Only 6.9% of them reported menarche before age 12 (Table 4.2).

A total of 153 (29.5%) women, who replied to a question regarding their menstruation replied that, they had completed menopause. Half of the women (51.6%) had regular menstruation. However, 18.9% of the women reported irregular menstrual bleeding. The median age of first sexual activity in women who respond to the question (n=322), was 21 (IQR, 18 to 24), ranging from 13 to 37. A total of 90 women (18%) reported early sexual activity (at age < 18 year).

The majority (76%) of participants had been at least once pregnant in their lifetimes (Table 4.2). Minimum age at first delivery was reported 14 and the maximum was 39. The median age of the first delivery in this study was 22 (IQR 19 to 26). The median number of deliveries in our study population was 2 (IQR, 2 to 3) ranging from 1 to 7. Only 9.2% of the women reported their first delivery age younger than 18 years, while a total of 78.9% reported their first delivery at the ages of 18 to 29 and 11.9% of them had their first delivery at ages older than 29 years (Table 4. 2). The median number of live births in the women participated in our study was 2 (IQR 2 to 3; max 6). More than one fifth of the women (21%) had experienced one or more miscarriages (median 1; Maximum 5). Among women who answered the questions about breast feeding, 70.5% had experienced breastfeeding.

The median period of breast feeding was 13.5 months (IQR 6 to 24 months). The overall period of breast feeding for women participating this study was ranged from a minimum 1 month to maximum 70 months.

Table 4. 2. Summary of descriptive values for personal reproductive variables

Variable (valid data)	Group	N (%)
Age at menarche (N=478) Median (IQR); 13 (12-14)	Age < 12	33 (6.9)
	Age 12-15	402 (84.1)
	Age >16	43 (9)
Menstruation (N=518)		
	No	153 (29.5)
	Yes, regular	267 (51.6)
	Yes, irregular	98 (18.9)
Pregnancy (N=516)		
	Yes	392 (76)
	No	124 (24)
Age at first delivery (N= 336) median (IQR), 22 (19-26)		
	<18	31 (9.2)
	18- 29	265 (78.9)
	> 29	40 (11.9)
Number of Delivery (n= 334) Median (IQR); 2 (2-3)		
	≤ 2	230 (68.9)
	3 --5	95 (28.4)
	≥ 6	9 (2.7)
Breast feeding (N=502)		
	Yes	354 (70.5)
	No	148 (29.5)
Age at first intercourse (N= 322) median (IQR), 21 (18-24)		
	≥18	264 (82)
	<18	58 (18)

Median BMI of our study population was 24.9 (IQR, 21.7 to 28.2). Of women in our study, 18.3% were obese, 31.1% were overweight and half (50.6%) of them had normal weight at the time of answering to the questionnaire.

In this study, 40 (7%) of women had a past history of cancer. The most common cancer was breast cancer with 15 women (37.5%) and only in 3 cases the diagnosis was uterine and cervical cancers. Considering

available data, median diagnosis age of cancer in these women was 44 years. Of 40 cancer positive women, about half of them (19 women or 47.5%) were still on treatment.

About 14% (n=85) of women in our study were hypertensive. More than half (54%) of these hypertensive women were taking regular medications to control their hypertension. Only 6.2% (n=37) of our study population were diagnosis diabetes mellitus and 7.9% of the women were osteoporotic, and only 1.2% of the women had a history of colorectal adenoma.

Of the women, 23.7% were regularly receiving analgesic/anti-inflammatories including aspirin.

For family history of cancer, a total of 65.9% reported a positive family history of cancer. Breast cancer was the most common type among them (Table 4.3), as 18.4% of the women had a family history of breast cancer. The frequency of all gynecologic cancers in the family history was 2.5% (in first degree relatives). About 27% of the women reported more than one case of cancer in their families (not only in first degree relatives, but also in distant relatives).

From the women who answered the question related to their current or past hormone replacement therapy (HRT), 82.4% replied in never, while 6.6% of them were using HRT for a median of 2.5 years (IQR, 1.5 to 10 years) at the time of replying the questionnaire. Almost 11% of participants was taking HRT for a median of 2 years (IQR, 1 to3 years) previously, and the median discontinuation time was 6 years (IQR 3 to 9 years).

Most (73.7%) of the women reported that they had never used OC pills (Table 4.3), 20.1% of them had used OC pills. Only 6.2 percent of the women was currently using these pills at the time of participating in this study. Median duration of the use of OC pills was 3 years (IQR, 1 to 5 years).

Table 4. 3. Summary descriptive values of personal/familial medical and drug history

Variable (valid data)	Group	Median (IQR)	N (%)
BMI (N= 453) median (IQR) 24.9 (21,7-28.2))	Age ≤ 35	21.5 (20-24.2)	110(24.3)
	Age = 36-55	25.4 (22.2-28.7)	234(51.7)
	Age ≥ 56	26.9 (24-30)	88 (19.4)
Interpretation of BMI (N=453)	Normal (BMI ≤ 25)		229 (50.6)
	Overweight (25.1-30)		141 (31.1)
	Obese (BMI ≥ 30.1)		83 (18.3)
History of chronic diseases	Cancer		40 (7)
	Hypertension		85(14.3)
	Osteoporosis		47 (8)
	Diabetes		37 (6.2)
	Colorectal adenoma		7 (1.2)
Family history of cancer (N= 551)			
	Yes		363(65.9)
	No		188 (34.1)
Cancer types in Family (N=326)			
	Breast		60 (18.4)
	Lung		48(14.7)
	Colorectal		32 (9.8)
	Gynecologic		15 (4.6)
	Liver		6 (1.8)
	Others		165(50.6)
Hormone Replacement Therapy (N=228)			
	Never		188(82.4)
	Yes, discontinued	2 yrs. (1-3)	25 (11)
	Yes, currently	2.5 yrs. (1.5-10)	15 (6.6)
Oral Contraceptive Pills (N=487)			
	Never		359(73.7)
	Yes, discontinued	2 yrs. (1-4.5)	98 (20.1)
	Yes, currently	3 yrs. (1-5.5)	30 (6.2)
Tamoxifen (N=433)			
	Never		421(97.2)
	Yes, discontinued	5 yrs. (3.5-5)	5 (1.2)
	Yes, currently	3 yrs. (1-3)	7 (1.6)
H/O Breast biopsy (N=493)			
	No		434 (88)
	Yes, don't know the result		14 (2.8)
	Yes, benign		32 (6.5)

H/O Mastectomy (N=484)	Yes, malignant	13 (2.6
	No	470 (97)
	Yes, unilateral	12 (2.5)
	Yes, bilateral	2 (0.4)
H/O Oophorectomy (N=491)		
	No	452 (92)
	Yes, unilateral	15 (3.1)
	Yes, bilateral	24 (4.9)
H/O STDs (N=470)		
	No	458(97.4)
	Yes	12 (2.5)
H/O STDs in partner (N=414)		
	No	412(99.5)
	Yes	2 (0.5)

H/O- History/of; BMI- Body Mass Index; STD-Sexually Transmitted Disease

The vast majority (97.2%) of women who replied the question related to history of tamoxifen answered as “never” (Table 4. 3).

The questionnaire also contains questions regarding some screening/diagnostic and therapeutic procedures for gynecologic/women problems. Twelve percent (n=59) of the women stated a previous breast biopsy, among them in 13 cases the histologic diagnosis was malignant (Table 4. 3). A total of 14 (2.9%) of the women participated in our study had a positive history of mastectomy. And 10 of the women said that, they had received chest radiography. Twenty-four women (4.9%) answered to these questions reported bilateral oophorectomy, while 15 (3.1%) had unilateral (Table 4. 3). There were no data about the causes of oophorectomy in these women.

When the women were asked about the past history of sexually transmitted diseases (STDs), the vast majority (97.4%) of them replied in “No”, and for their partners, 99.5% of women answered that their partners never have had STDs.

Majority (64.6%) of the women reported themselves as current or past cigarette smokers. Median duration of smoking was 18 years (IQR, 10

to 25 years). They reported to smoke a median number of 20 (IQR, 10 to 20) cigarette per day. Seventy-three percent of women who respond a question about passive smoking, submitted passive smoking. Median daily hours of exposure to smoke was 5 (IQR, 2 to 8) hours.

The majority (70.9%) of women in this study reported that they do not drink alcohol. Women were asked about their dietary habits.

About 52.6 % of women participating in this study had used red meat once or less than once in a week, only 1.1% (n=6) of them mentioned themselves as vegetarians. Of the women, 46.4% stated that they are used to eat red meat 2 or more times in a week.

About 35.4% of the women were used to consume less than one portion of fresh vegetable/ fruit in a day. And only 16.6% of them said to eat 3 or more portions of fruits/vegetables daily.

Of the women, 12.5% reported that they eat salty/smoked foods every day, and 24.6% of them once or more in a week. However, the majority (62.9%) of our population said, they might use this kind of foods once in months or never.

Answering about their sport habits, only 11% of our study population reported that they exercise regularly. However, about half (49.2%) of the women who answered this question stated that they never do sport (Table 4. 4).

A total of 265 (88.9%) of the women had one sexual partner. Only 9.1% of them reported 2-4 sex partners, and 2% of them had more than 4 sexual partners in their lives. The median number of sexual partners was 1 person. Considering the available data about protective usage of condom, only 9% of the women reported that, they use it always, while 62.1% of them had never used it (Table 4.4).

About 8.1% of the women had no awareness about mammography, and 33.1% of the women neither had the test in the past, nor have a plan to do it in the future. However, 21% of women in our study had mammography in the past and have planned to repeat the test in the future (Table 4.4 and figure 4.1).

Table 4.4. Summary descriptive values of behavior/ awareness variables

Variable (valid data)	Group	N (%)
Smoking (N=495)	Yes, now/past	320 (64.6)
	No	175 (35.4)
Sport habits, weekly (N= 498)		
	Professionally	2 (0.4)
	Regularly	55 (11)
	Sometimes	80 (16.1)
	Rarely	116 (23.3)
	Never	245 (49.2)
Number of sex partners (N=298)		
	One	265 (88.9)
	2--4	27 (9.1)
	> 4	6 (2)
Condom use (N= 377)		
	Never	234 (62.1)
	Sometimes	79 (21)
	Often	30 (8)
	Always	34 (9)
H/O Mammography (N=480)		
	No awareness	39 (8.1)
	No, don't want to do	159 (33.1)
	No, going to do	89 (18.5)
	Yes, will not repeat	91 (19)
	Yes, will repeat	102 (21.3)
H/O Pap test (N=479)		
	No awareness	82 (17.1)
	No, don't want to do	133 (27.8)
	No, going to do	49 (10.2)
	Yes, will not repeat	106 (22.1)
	Yes, will repeat	109 (22.8)

A total of 82 (17.1%) of the women participating in this study had no awareness about Pap smear. While 22.8% of them did the Pap test in the past and had a plan for future to repeat it (Table 4.4 and figure 4.2).

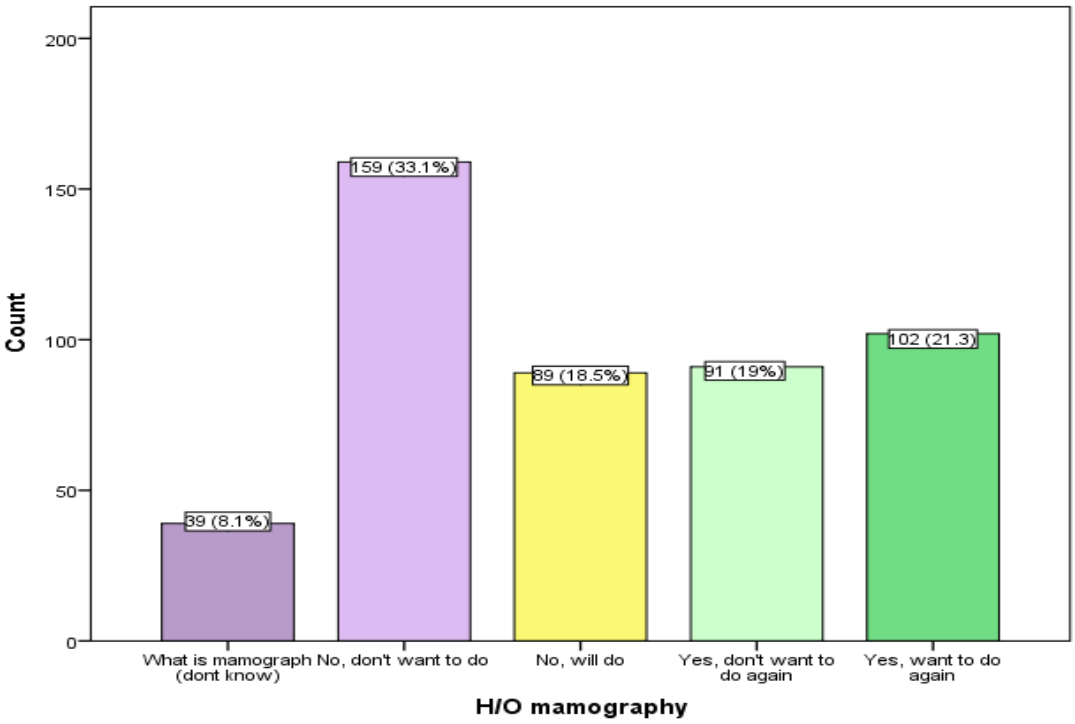


Figure 4.1. The women's awareness and behavior about mammography

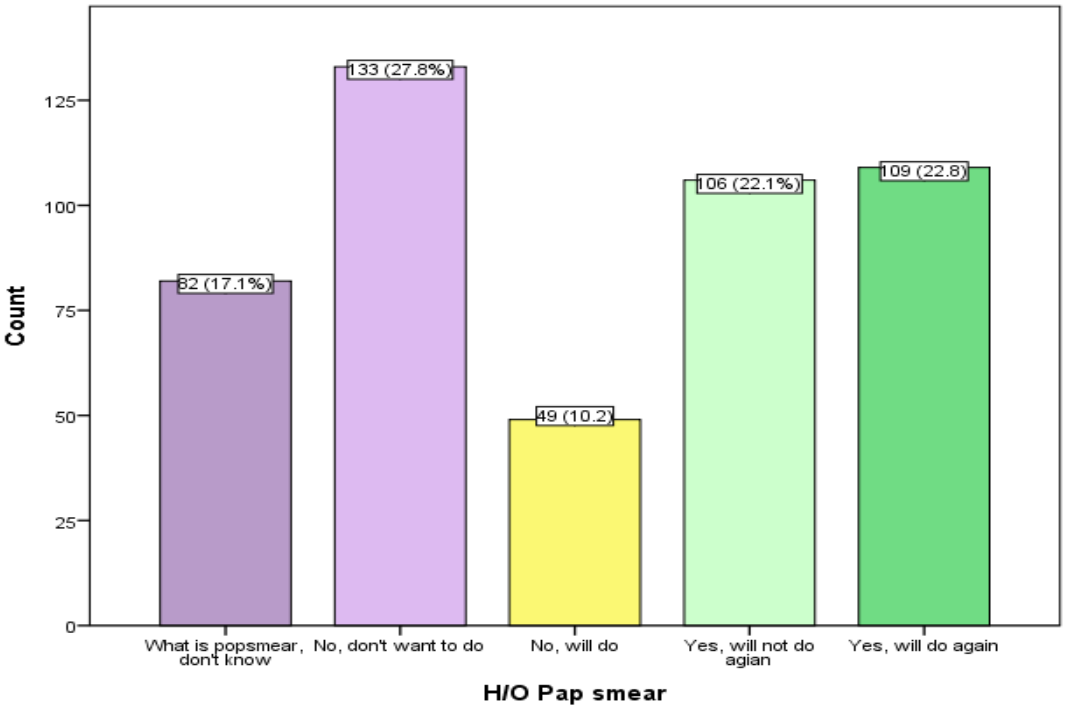


Figure 4. 2. The women's awareness and behavior about Pap Test

As aging is an important risk factor for most of gynecologic, we have searched for any age variations in groups of women with some particular characteristics (Table 4.5). We found significantly higher median age in women with menstrual irregularity compared with regularly menstruating women (p=0.001). Groups of women according to their sport habits were compared and it was found that, compared to women in sometimes exercising groups, women with rarely exercise habits were significantly younger (p=0.001,) for details see table 4.5. Compared to those with normal weight, women in obese group were more likely to be older (p<0.001).

There was no evidence of significant median age difference between smokers and non-smokers in this study (Table 4. 5). Also, no significant variation between different age groups in relation to the number of sex partners was found.

Table 4.5. Age variations in different groups.

Variables	Median age (IQR)		P-value
Menstruation			
- No	58	(54-63)	P= 0.001
- Yes, Regular	39	(32-45)	
- Yes irregular	45	(35-50)	
Smoking			
- Yes	44	(36-53)	P= 0.544
- No	46	(33- 56)	
Sport habits			
- Professional (n=2)	36.5	-	P=0.004
- Regularly	47	(39-55)	
- Sometimes	49	(39-57)	
- Rarely	42	(32-52)	
- Never	44	(35-54)	
BMI			
- Normal	40	(32-48)	P<0.001
- Overweight	50	(42-56)	
- Obese	53	(45-58)	

To compare the age of menarche in different age groups, all women were divided into four age groups of (15-25), (26-45), (46-66), and older

than 66. Median age at menarche did not vary significantly among the groups of women participating in this study.

We found no significant difference in breastfeeding practice, age at first delivery and age at first intercourse between the age groups. The median age of women with early sex activity (age <18) was not significantly different from women with first sexual activity > 18 years of age.

After comparing BMI of women having regular menstruation with women of the irregular menstruating group (Table 4. 6), we found that women with irregular menstruation were more likely to have a higher BMI ($p<0.001$).

Higher percentage of women in the smoker group had a normal BMI compared to non-smokers ($p=0.014$). The proportion of overweight in both smokers and non-smokers was not significantly different. However, obesity was found to be significantly higher in non-smokers (Table 4. 6). When compared BMI in different cohorts of marital status in this study population, we found most single women were in the normal ranges of BMI (67% normal weight compared to 5.6 % obese). Proportion of obesity was significantly lower in singles compared to others ($p<0.001$). Prevalence of obesity was highest in widows (36.8%) especially versus singles (5.6%).

A higher proportion of hypertensive women were overweight and obese compared to normotensive women. This difference in women with diabetes was more significant. No difference in obesity proportions according family history of cancers. No association between family history of cancer and obesity was found ($p=0.268$). Moreover, BMI was not different according HRT and use of OC pills (Table 4. 6). The percentage of obesity was not significantly different between women who had breast biopsy from those had not (54% vs. 48%, respectively). Compared to normal BMI holders, a larger proportion of women with a history of bilateral oophorectomy were obese (17.7% vs. 43.5%, respectively).

We found that a higher proportion of women complaining from osteoporosis was included in pregnancy positive group ($p=0.029$), same as

other chronic disease (Table 4. 6). Use of OC was significantly higher in ever pregnant women compared to the group of women, who never had been pregnant (p<0.001). On the other hand more women with benign breast biopsy had one or more pregnancies versus malignant ones (96.9% vs. 76.9%).

Table 4.6. BMI and pregnancy status variations according other variable

	N	BMI - N (%)				N	Pregnancy - N (%)		
		< 25	25.1-30	> 30.1	P- value		No	Yes	P- value
Chronic Diseases									
- Diabetes	27	1 (3.7)	11 (40.7)	15(55.6)	P<0.001	31	3(9.7)	28 (90.3)	P=0.001
- Hypertension	69	15 (21.7)	21 (30.4)	33(47.8)	P<0.001	71	5 (7)	66 (93)	P<0.001
- Osteoporosis	39	18 (49)	10(25.6)	11 (28.2)	P=0.202	40	4 (10)	36 (90)	P=0.029
- CR adenoma	4	2 (50)	2 (50)	0 (0)	P=0.548	5	0 (0)	5 (100)	-
Menstruation									
- Regular	240	129(63)	55(27)	20 (10)	P<0.001	264	90(34)	174(66)	p<0.001
- Irregular	74	36 (48.6)	23 (31.1)	15 (20.3)		96	22(22.9)	74 (77.1)	
Marital status									
- Single	90	71 (78.9)	14 (15.6)	5 (5.6)	P<0.001	102	95(93)	7 (6.9)	p<0.001
- Married	297	131(44)	107 (36)	59 (19.9)		338	23 (7)	315(93)	
- Divorced	32	14 (43.8)	9 (28.1)	9 (28.1)		35	3 (8.6)	32 (91.4)	
- Widow	19	7 (36.8)	5 (26.4)	7 (36.8)		15	0 (0)	15 (100)	
HRT									
- No	134	50 (37.3)	48 (35.8)	36 (26.9)	P=0.522	183	27(15)	156(85)	P=0.27
- Yes	31	15 (48.4)	6 (19.4)	10 (32.2)		40	4 (10)	63 (90)	
OCP									
- No	275	139(50)	83 (30.7)	53 (19.3)	P=0.623	356	99(28))	257(72)	p<0.001
- Yes	105	57 (54.3)	29 (27.6)	19 (18.1)		125	15 (12)	110 (88)	
Breast biopsy									
- No	333	176(53)	93 (27.9)	64 (19.2)	P=0.14	429	109(25)	320(745)	P=0.04
- Yes, unsure*	12	8 (66.7)	2 (16.7)	2 (16.7)		14	4(28.6)	10 (71.4)	
- Yes, benign	28	13 (46.4)	11 (39)	4 (14.3)		32	1 (3.1)	31 (96.9)	
- Yes, malignant	10	2 (20)	3 (30)	5 (50)		13	3 (23)	10 (77)	
Oophorectomy									
- No	345	182(52)	102(30)	61 (18)	P=0.033	444	114(25)	331 (75)	P=0.01
- Yes, unilateral	12	7 (58.3)	2 (16.7)	3 (25)		15	2(13.3)	13 (86.7)	
- Yes, bilateral	23	7 (30.4)	6 (26.1)	10 (43.5)		24	0 (0)	24 (100)	
Cancer in family									
- No	150	83 (55.3)	42 (28)	25 (16.7)	P=0.128	170	45 (27)	125 (73)	P=0.44
- Yes	76	130(47)	91 (33)	55 (19.9)		326	76 (23)	250 (77)	
Smoking									
- No	129	58 (45.5)	38 (30.2)	32 (24.3)	P=0.035	159	44(28)	115(72)	P=0.28
- Yes	255	140(55)	78 (30.6)	37 (14.5)		290	66(23)	224(77)	
Monthly income									
- < 500	25	10 (40)	11 (44)	4 (16)	P=0.019	34	8 (23)	26 (76.5)	P=0.86
- 500-1000	127	52 (40.9)	45 (35.4)	30 (23.6)		151	37(25)	114(75)	
- 1000-3000	221	117(53)	64 (29)	40 (18.1)		249	64(26)	185(74)	
- >3000	44	31 (70.5)	10 (22.7)	3 (6.8)		50	10 (20)	40 (80)	

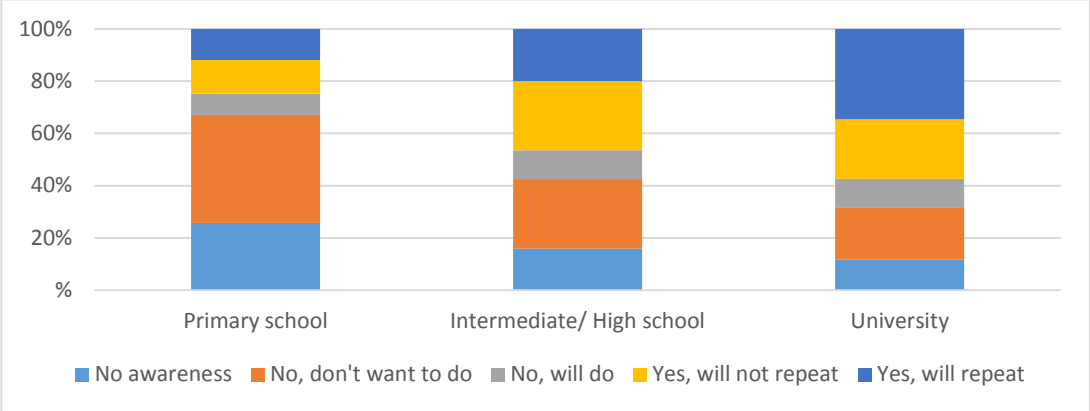
*women were not sure about the pathologic nature of the taken breast sample.

In this study, the prevalence of obesity in women with a monthly income more than 3000TL was lower compared to other groups (p=0.019). Also lower prevalence of obesity was observed in higher educated women

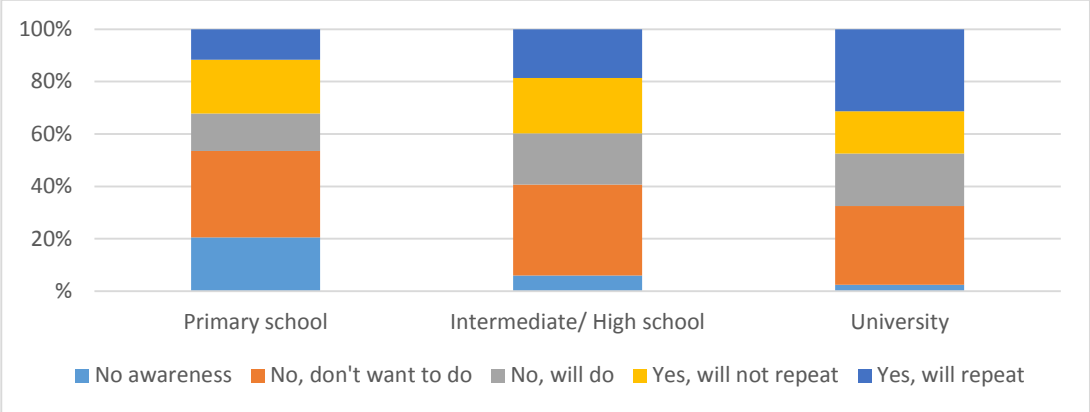
(university or more) compared to those with primary education (10.9 vs. 35.7%). We found that women with higher levels of education (university, master and PhD) had the highest levels of awareness about Pap test (88%) and mammography (97%). This difference was statistically significant (p<0.001). The women with higher education had done the test before and said, will repeat the tests again in the future (Table 4.7; figure 4. 3). Most of the women with primary or lower education had no awareness of the screening tests and/or had no intention to do it.

Table 4.7. Women's awareness and behavior about screening tests and condom use, according their level of education

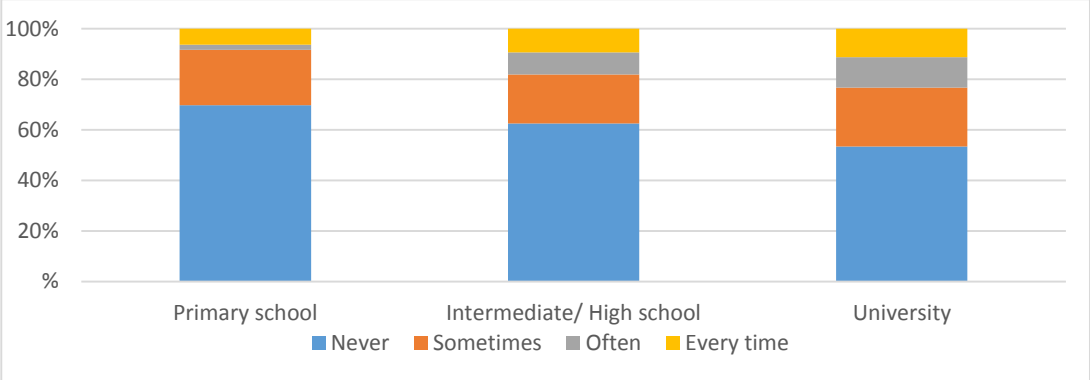
			Levels of education N (%)			
		N	< Primary school	Intermediate/high school	University +	P-value
Pap smear	No awareness	79	28 (35.4)	32 (40.5)	19 (24.1)	P<0.001
	No, don't want to do	130	45 (34.6)	53 (40.8)	32 (24.6)	
	No, will do	49	9 (18.4)	22 (44.9)	18 (36.7)	
	Yes, will not repeat	104	14 (13.5)	53 (40)	37 (35.6)	
	Yes, will repeat	109	13 (11.9)	40 (36.7)	56 (51.4)	
Mammography	No awareness	39	23 (59)	12 (30.8)	4 (10.3)	P<0.001
	No, don't want to do	154	37 (24)	69 (44.8)	48 (31.2)	
	No, will do	87	16 (18.4)	39 (44.8)	32 (36.8)	
	Yes, will not repeat	91	23 (25.3)	42 (46.2)	26 (28.6)	
	Yes, will repeat	100	13 (13)	37 (37)	50 (50)	
Condom Use	Never	229	67 (29.3)	100 (43.7)	62 (27.1)	P<0.048
	Sometimes	79	21 (26.6)	31 (39.2)	27 (34.2)	
	Often	30	2 (6.7)	14 (46.7)	14 (46.7)	
	Always	34	6 (17. 6)	15 (44.1)	13 (38.2)	



A) Pap smear



B) Mammography



C) Condom use

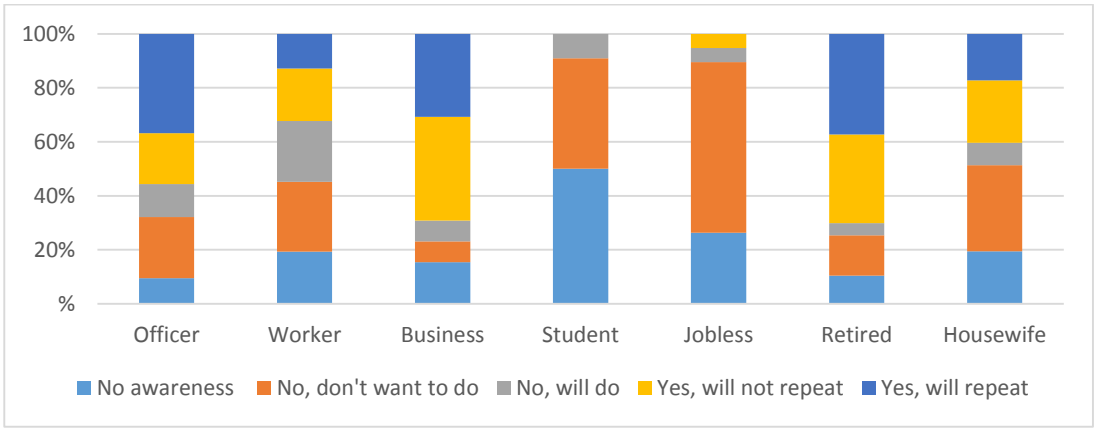
Figure 4.3. Women awareness/behavior about A) Pap smear; B) mammography; and C) condom, according their level of education

The condom was used less frequently in women's group with lower education level, while women with higher education reported a more frequent usage of it (Table 4. 7 and figure 4. 3). But the difference was not significant.

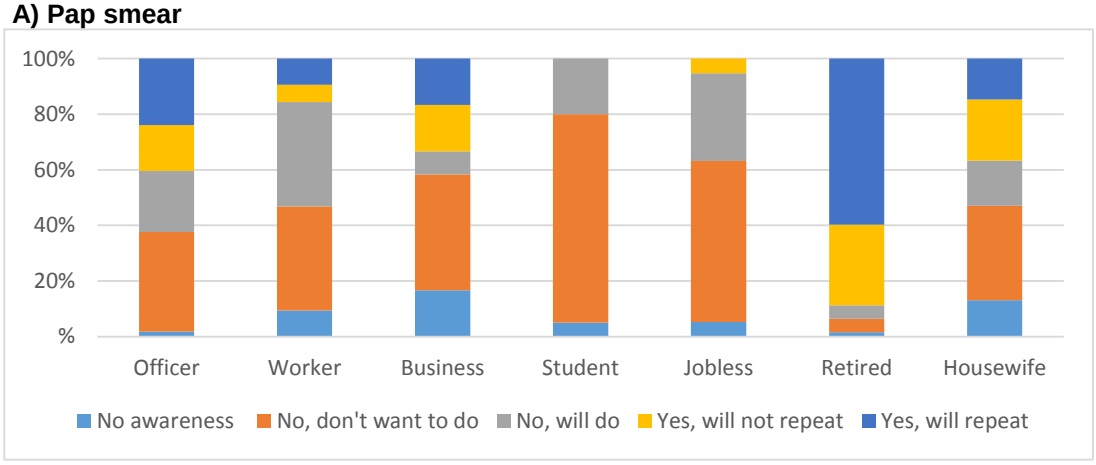
Overall awareness about Pap test was lower than for mammography in women with different employments. About 38% of retired women had done Pap test and had planned to repeat it in the future, this percentage for mammography was 59.7% in retired women. (Table 4. 8; Fegure 4.4)

Table 4.8. Women's awareness and behavior about screening tests and condom use, according their employment status.

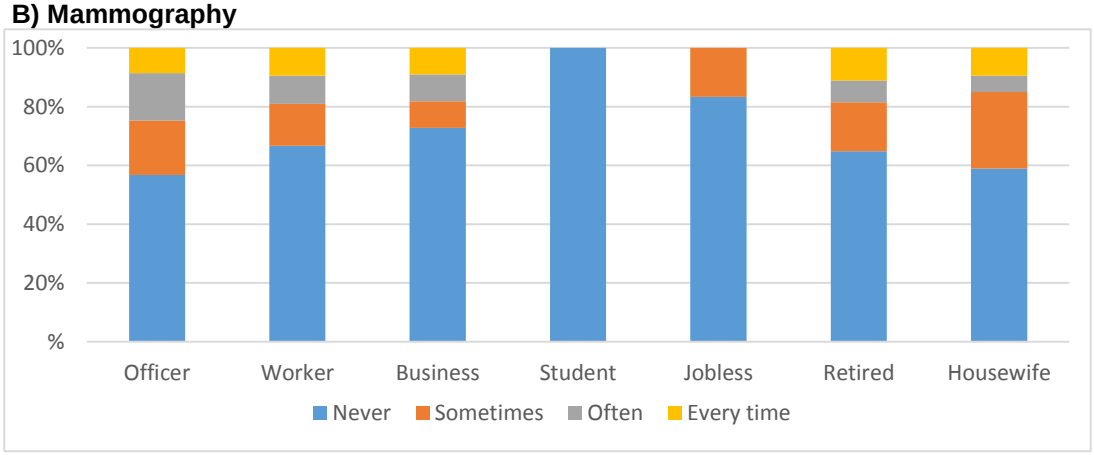
	Employment N (%)							
	Officer	Worker	Business	Student	Jobless	Retired	H.W	N
Pap smear								
No awareness	10 (12.8)	6 (7.7)	2 (2.6)	11 (14.1)	5 (6.4)	7 (9)	37 (47.4)	
No, don't want to do	24 (19.1)	8 (6.4)	1 (0.8)	9 (7.2)	12 (9.6)	10 (8)	61 (48.8)	
No, will do	13 (30.2)	7 (16.3)	1 (2.3)	2 (4.7)	1 (2.3)	2 (7)	16 (37.2)	P<0.001
Yes, will not repeat	20 (20.4)	6 (6.3)	5 (5.1)	0 (0)	1 (1)	22 (22.4)	44 (44.9)	
Yes, will repeat	39 (37.1)	4 (3.8)	4 (3.8)	0 0)	0 (0)	25 (23.8)	33 (31.4)	
Mammography								
No awareness	2 (5.7)	3 (8)	2 (5.7)	1 (2.9)	1 (2.9)	1 (2.9)	25 (71.4)	
No, don't want to do	39 (26)	12 (8)	5 (3.3)	15 (10)	11 (7.3)	3 (2)	65 (43.3)	
No, will do	24 (29.6)	12 (14.8)	1 (1.2)	4 (4.9)	6 (7.4)	3 (3.7)	31 (38.3)	P<0.001
Yes, will not repeat	18 (21.7)	2 (2.4)	2 (2.4)	0 (0)	1 (1.2)	18 (21.7)	42 (50.6)	
Yes, will repeat	26 (27.1)	3 (3.1)	2 (2.1)	0 (0)	0 (0)	37 (38.5)	28 (29.2)	
Condom use								
Never	46 (21.2)	14 (6.5)	8 (3.7)	3 (1.4)	5 (2.3)	35 (16.1)	106 (48.8)	
Sometimes	15 (19.7)	3 (3.9)	1 (1.3)	0 (0)	1 (1.3)	9 (11.8)	47 (61.8)	
Often	13 (43.3)	2 (6.7)	1 (3.3)	0 (0)	0 (0)	4 (13.3)	10 (33.3)	P=0.585
Always	7 (21.2)	2 (6.1)	1 (3)	0 (0)	0 (0)	6 (18.2)	17 (51.5)	



A) Pap smear



B) Mammography



C) Condom use

Figure 4. 4. Women awareness/behavior about: A) Pap test; B) mammography; and C) condom use according their employment status

Second most motivated women toward screening tests were officers and business women. A great proportion of jobless women and students neither had done the screening tests, nor had plan to do them. Non of students had plan to do the tests in future (Fegure 4. 4). The housewives

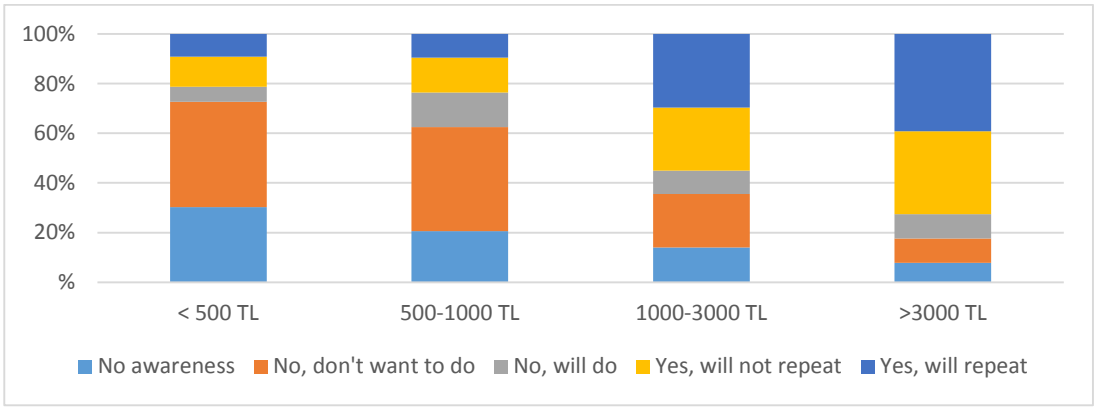
not only constituted majority of unawared women (47.4% for Pap test; 37.2 for mammography, but also a great percentage of them had no plan to do Pap test and mammography in future too. Detailed information is provided in (Table 4.8) and (Figure 4.4). Most of the women in all employment groups had never used condom. All (100%) of students never uesed it. About 57% of officers never used condom, which was not significatly different from what was found for housewives (59%), for details see Figure 4.4.

Women with the lower income (<1000TL) had the least awareness about the screening tests compared to others (Figure 4. 5). Even if they were awared, compared to others a considerable

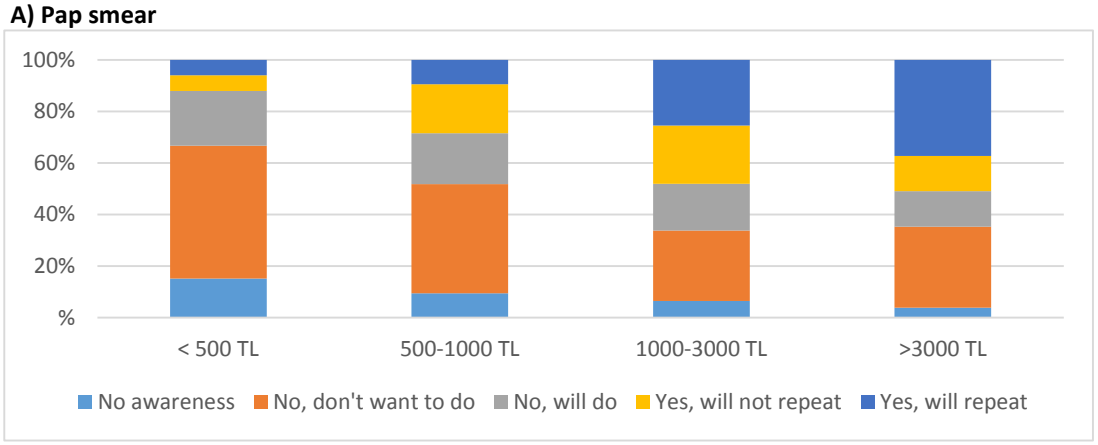
Table 4. 9. Women's awareness and behavior about screening tests and condom use in groups of different monthly income

		Monthly income N (%)				
		<500 TL	500-1000TL	1000-3000TL	>3000 TL	P-value
Pap smear N=456	No awareness	10(13.3)	28(37.3)	33 (44)	4 (5.3)	
	No, don't want to do	14 (11)	57 (44.9)	51 (40.2)	5 (10.4)	
	No, will do	2 (4.2)	19 (39.6)	22 (45.8)	5 (10.4)	P<0.001
	Yes, will not repeat	4 (4)	19 (19)	60 (60)	17 (17)	
	Yes, will repeat	3 (2.8)	13 (12.3)	70 (66)	20 (18.9)	
Mammography N=452	No awareness	5 (14.3)	13 (37.1)	15 (42.9)	2 (5.7)	
	No, don't want to do	17 (11)	58 (37.7)	63 (40.9)	16 (10.4)	
	No, will do	7 (8.4)	27 (32.5)	42 (50.6)	7 (8.4)	P<0.001
	Yes, will not repeat	2 (2.3)	26 (29.9)	52 (59.8)	7 (8)	
	Yes, will repeat	2 (2.2)	13 (14)	59 (63.4)	19 (20.4)	
Condom Use N=356	Never	17 (7.9)	66 (30.8)	113 (52.8)	18 (8.4)	
	Sometimes	6 (7.6)	31 (39.2)	31 (39.2)	11 (13.9)	P=0.001
	Often	1 (3.3)	4 (13.3)	15 (50)	10 (33.3)	
	Always	0 (0)	7 (21.2)	22 (66.7)	4 (12.1)	

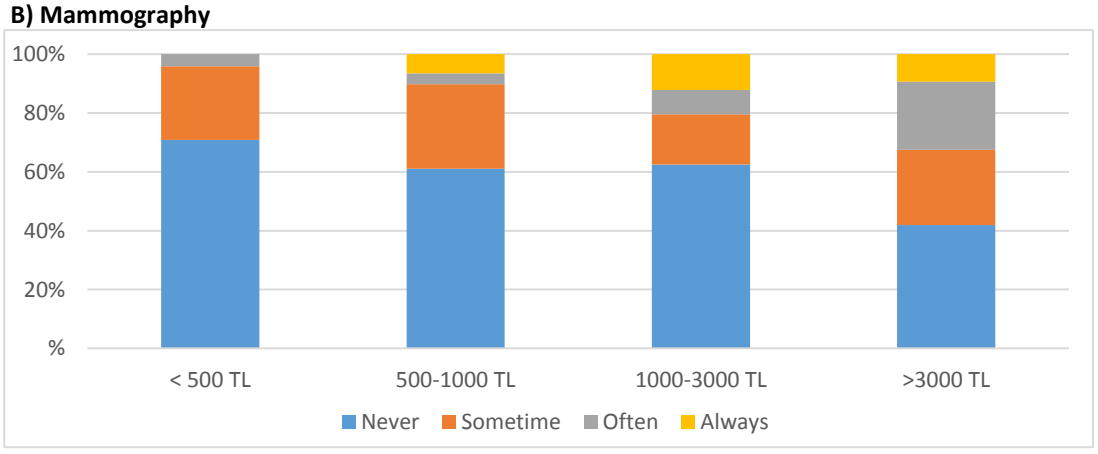
percentage of them had no plan to do the Pap test (42.4% & 41%) or mammography (51.5% & 41%), see figure 4.5. This finding was statistically significant ($p<0.001$). Also, condom use was lowest in groups of women with lower monthly income (Table 4.9; Figure 4.5).



A) Pap smear



B) Mammography



C) Condom use

Figure 4. 5. Women awareness/behavior about A) Pap smear; B) mammography; and C) condom use in groups of different monthly income

5. DISCUSSION

This study is an initiative effort to measure frequency of specific gynecologic cancer risk factors in female relatives of cancer patients who were treated in Hacettepe University Oncology Hospital.

The mean (SD) age at interview for the participants was 45.7 (12.2) years. About 76% of the women were older than 35, mostly (90%) living in urban areas, and 31.8% of them were university or higher level graduates. Comparing to Turkish general population (female median age of 29.6) the women participating in this study were older (1), and more likely to live in cities (71.5% of the Turkish general population are urban) (46). Compared to given data about Turkish general population for smoking (overall 27%; female 13%) percentage of smoking (current/past) in our study population was higher (64.6%). There could be some explanations for this difference, such as; higher median age, higher urbanization, and higher levels of education in our study population. However, as smoking is a modifiable cancer risk factor, population should be encouraged to quit smoking for cancer prevention, especially if they have some unmodifiable cancer risks, e.g. family history of cancer.

Median menarche age was 13 years and was higher than what Chumlea WC *et al*. found for U.S white girls whose median age at menarche was 12.6 years (47) . Median age at menarche in this current study confirms findings of Ekerbicer H C *et al*., in their study about age at menarche in adolescents in the Eastern Mediterranean city of Kahramanmaras, Turkey, who recorded age at menarche as 13 years (95%CI: 12.97- 13.03). According to this study the probability of menstruating before the age of 11.5 years was 10% (48). In our study only 6.9% had early menarche (<12 years). For American girls this percentage was more than 10%, (47) . In 2009 Talma *et al*. reported that, 33% of Turkish girls living in Netherland had early menarche (49).

Median age at first intercourse in this study was 21 years, and only 11.1% of participants reported sexual activity before age of 18, which is a

high risk behavior toward HPV infection and subsequent increase in the risk of cervical cancer. In a study of Dagdeviren N *et al.* (2004-2005), about sexual activity among Turkish adolescents (median age 18 yrs.), it was found that the median age of sexual activity in girls was 17 years, near to Western countries (mean±SD; 16.7±1.8) (50). The possible explanation of this difference is the possibility of changes in sexual behaviors over the time period. But this prediction needs further investigations for evaluating any changes of sexual behavior in the Turkish general population.

The majority of the women in our study had one sexual partner, and only 11.1% of them had an experience of two of more. Available data from this study indicates a lower (2.5%) prevalence of STDs in participants. Having one sexual partner can explain the lower rate of STDs, but there is a high chance of recall bias (the women may forget their past diseases), and nonresponse (all women did not reply to the question). Only 0.5% of them report a past diagnosis of STDs in their partners. According to WHO, the global prevalence of HIV/AIDS among people aged from 15 to 49 (2012) was 0.8 (95%CI, 0.7-0.9). While, prevalence of Trichomonas vaginalis in European region was estimated 8%, Chlamydia trachomatis 1.1%, Syphilis 0.5%, and Neisseria gonorrhea 0.3% (1). We were unable to compare our rates with the WHO reports, because of the lack of the exact diagnosis of STDs in our study. But we concluded that the rate of STDs was relatively low when compared to the World data.

Sixty-two percent of women in this study, told that they never use the condom, while, 9% always used it. Women with lower education levels had a lower rate of condom usage. Students and housewives had the least condom usage, however; its usage was better in employed women compared to unemployed ones. Also, women in low income groups had a lower condom use compared to others. But, to prevent cervical cancer, modifying population’s awareness and behavior toward condom usage is vital.

Most (67.9%) of the women were married, 76% of the women had the history of at least one pregnancy by the time participating in the study.

Use of the OCP was higher in ever pregnant women compared to those never pregnant. More women in the irregular menstruating group had been pregnant compared to those with regular menstruation (77.1% vs. 65%).

Median age at first delivery was 22 and the rate of early delivery was 9.2%, which is higher than what is found in Europe (1% in Germany, 2% in France), consistent with the United States (10%) and lower than in Mali (45%), in Uganda (42%), Ethiopia (25%) (51). The cultural aspect of women's sexual and productive life shows its effects in different manners through the world, and when we compared our rates with our neighboring continent, Europe, we found that the early delivery rates were significantly higher, which may reflect the imprints of Asian culture in the daily living of our society. Early marriages, and child brides are one of the major public health problems of our country.

Median number of deliveries in women participating in the study were 2 children. 70% of the women had positive breastfeeding history, the median period of total breastfeeding was 13.5 months for all their children. Of ever pregnant women participating in this study, 8.8% had no experience of breastfeeding. While according to WHO data for Turkey (2010) 96.7% of infants have had breast feeding (52).

About 26.3% of the women had used oral contraceptive pills. Of them only 6.1% were currently using the pills. Median OCP taking duration was 3 years (IQR, 1-5).

In this study, 29.5% of women had completed their menopause. Besides, more women with irregular menstrual bleeding were obese and overweight, when compared to normal menstruating women.

Women in this study had a median BMI of 24.9. According to the documented BMI 31.1% overweight, and 18.3% were obese. In recently provided data by the World Health organization in the European Region (including Turkey) rate of overweight adults were between 30% - 70%, and 10-30 percent of the population in these countries was obese (1) . While in 2008 it was estimated that in Turkey proportion of obesity would be 35.6% (95%CI; 32-39.4) (1).

Women in obese group were significantly older compared to those with normal weight. We found that, obesity was more prevalent in nonsmokers when compared to those who smoke. But, women with higher education (university or more) and high income (more than 3000 TL) had lower obesity percentages (6.8% and 10.9% respectively) compared to others.

About half of the women reported that, they never make exercise. Compared to older women, those with younger age reported exercising less frequently. A considerable percentage in our study had a non-healthy diet (35% low fruit/vegetable, 46% high red meat consumption, and 37% high salted/smoked food consumption).

About 7% (n=40) of the women had a positive past cancer history, of them 15 women were breast cancer survivors, and 3 of them had uterine corpus/ cervix cancers.

All participants in this study came to the hospital with their relatives, who were cancer patients, but some of the cancer patients were not family members of the women (i.e. husband). As a result all of the women had not positive family history of cancer. About 66% of the participants had at least one family history of cancer in first degree relatives. Breast cancer had the highest (18.4%) proportion and second most common cancer in the family history was lung cancer, colorectal cancer was the third (9.8%) one, and gynecological cancers were the 4th (4.6%) common type in their families.

Although data about chronic diseases in our study was limited, we found that, among the women, 14.3% were hypertensive, 6.2% diabetic, and 8% were osteoporotic. Given data by WHO shows that age adjusted estimates for hypertension in Turkey (2008) was 24% (95% CI; 19.4-30.5), and for diabetes was 9.8% (95%CI; 6.8-13.2). These rates were higher than the rates observed in our population. We also found that, women with chronic diseases were older, and had higher BMI compared to those without the diseases.

Usage of hormone replacement therapy in the present study population was 16.6%. In addition 2.8% of the women had used tamoxifen.

About 12% (n=59) of women had a positive history of breast biopsy. Of them, 13 patients (2.6%) had a malignant histologic diagnosis, 8 of these women with malignant breast biopsy had a BMI more than normal range. In women with benign breast biopsy, pregnancy rates were higher when compared to malignant group.

Fourteen (2.4%) women participated in this study had mastectomy, and only in 2 cases it was bilateral. Compared to mastectomy, more women (8%, n=39) had oophorectomy, and 24 of the cases had bilateral procedure.

About 8.1% of participants in this study were not aware of mammography, 40.3% did it in past, and 39.8% of our study population had a plan to do it in future (21.3% repeating; 18.5% for the first time).

Awareness about Pap test was lower than mammography, 17.1% of the women had no awareness about Pap test. About 45% of the women had done it in past, and 33% had a plan to do it in future (22.8% repeating; 10.2% for the first time).

Compared to others, women with higher levels of education (university, Master and PhD) had the highest levels of awareness about Pap test (88%) and mammography (97%).

Awareness about the Pap test and mammography were different between employment groups. About 38% of retired women had done Pap test and had planned to repeat it in the future, and for mammography this figure was 59.7%. A great percentage of unemployed population, including housewives, had no awareness about both screening tools. Even if they were aware, a considerable proportion of them had no plan to do screening tests in the future.

Awareness and intention to do screening tests were lower in women with monthly income of lower than 1000 TL, when compared to others. Women with higher monthly income had a better awareness and behavior about screening tools.

All above findings show women with a higher education, working level and better income, have better awareness and behavior toward the available screening tools for gynecologic cancers.

From the findings in this study we can provide important descriptive information on the distribution of some risk factors for gynecologic cancers. Information available from this study could be used in developing more precise and specific data collection tools for future studies. Also, it can be used as the first step in the process of specific risk assessment tool development for Turkish women. This study had a nonrandom sampling design. As this study was done on a population with a specific condition (relatives of cancer patients), the results could have some variations from what is valid for the general population. However, findings from this study will be valid for similar population groups, such as; relatives of cancer patients.

We also some had some limitations in our study: All data were collected by applying a self-reported questionnaire, potentially contributing to measurement and recall errors. Besides, responses to all questions were not complete. Lastly, data reported here are cross-sectional and do not allow evaluation of causal relationships between variables.

Considering our findings, there were a variety of reproductive cancer risk factors in female relatives of cancer patients. Some of them like aging, family history of cancer, could not be prevented of modified while, some others could be modified to prevent cancer, such as; smoking, diet condom use, and exercise. So, population's awareness/behavior about cancer prevention should be improved.

For early detection and secondary prevention of cancers efforts should be done to increase awareness of women about screening tools and motivate them to take benefit of those tools continuously.

Further studies are needed to measure prevalence of the reproductive cancer risk factors in the Turkish general population. Besides, evaluation of general population's awareness and behavior about available screening tools are important. Finally, data from this study and similar studies can be used in developing cancer risk assessment tools, and strategies for cancer prevention.

6. CONCLUSION

Compared to the general population of Turkey, women participating in this study were more likely to be older. Percentage of some risk factors such as; early menarche, early sexual activity, and early child birth was lower than what was estimated in the literature. While, the prevalence of some others like obesity or some chronic disease were almost adherent to what is suggested in the literature. However, this study has also documented high tobacco use, low protective condom use and low rates of physical activity. We found that awareness and behavior of women were different according to their education, occupation, and monthly income.

These findings indicate a need for further and more generalized studies in order to understand local characteristics and distribution of gynecological cancer risk factors in Turkey. In addition, our findings support required efforts to increase general population awareness about available cancer screening tools. Also, there is a need for motivating women to use available screening tools according to the given guidelines.

By modifying diet and lifestyle, many of the cancers can be prevented. The results of this study appear the requirement of diet, lifestyle and exercise modifications for cancer prevention.

Finally, to our knowledge, there has not been any study conducted in Turkey regarding the prevalence of the known risk factors this study can be used as a primary step for further complete and general population surveys. The study provides information that will be useful for developing more specific and precise data collection tools specially for measuring risk factors of women’s cancers.

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Appendix 1. Questionnaire

HACETTEPE ÜNİVERSİTESİ ONKOLOJİ ENSTİTÜSÜ
PREVANTİF ONKOLOJİ ANABİLİM DALI
KANSER RİSKİ DEĞERLENDİRME FORMU

Sayın hastamız,

Bu anket, kişisel kanser riskinizi belirlemeye yönelik sorulardan oluşmaktadır. Yapacağımız değerlendirmenin sağlıklı olabilmesi için, vereceğiniz bilgilerin olabildiğince doğru ve eksiksiz olması büyük önem taşımaktadır. Anlamadığınız veya nasıl doldurmanız gerektiğine karar veremediğiniz bir soruyla karşılaşırsanız, bir görevli size yardımcı olacaktır. Cevaplamak istemediğiniz sorular olursa, bunları boş bırakabilirsiniz. Verdiğiniz bilgiler mutlak surette gizli tutulacak ve hiç bir şart altında başka şahıslara veya kurumlara iletilmeyecektir.
Verdiğiniz bilgiler, kimliğiniz tamamen gizli kalmak kaydıyla, bölümümüzce yürütülen bilimsel araştırmalarda kullanılabilir.

A - Kişisel Bilgiler

Ad: Soyad:
Hacettepe dosya no : _____ T.C. Kimlik No:_____
Doğum tarihi : __ /__ /__ (Gün/Ay/Yıl)
Cinsiyet: ☐ Erkek ☐ Kadın
Boy: __ cm Ağırlık: __ kg (İsterseniz, boy ve kilonuzu ölçebiliriz.)
Adres:

Posta kodu: Şehir: _____

Ev telefonu: (__) _____
İş telefonu: (__) _____
Cep telefonu: (__) _____
E-mail: _____@_____

Bölümümüz takip ettiği kişilere, belirli aralıklarla kanserden korunmayla ilgili güncel konular ve yeni bilimsel gelişmeler hakkında bilgilendirme mesajları göndermektedir. E-mail adresinizin bu listeye eklenmesiyle herhangi bir reklam mesajı almayacağınızdan emin olabilirsiniz. E-mail adresiniz hiç bir şart altında üçüncü bir şahıs veya kuruluşa iletilmeyecektir. Bölümümüzden bilgilendirme mesajları almak ister misiniz?
☐ Evet ☐ Hayır

Medeni durum
☐ Bekar ☐ Evli ☐ Boşanmış ☐ Dul

Doğum yeriniz (il / ilçe): _____ /_____
Bugüne kadar en uzun yaşadığınız yer (il / ilçe): _____ /_____
☐ Kırsal ☐ Kentsel

Kat No. | **427857**

Mesleğiniz (Mesleki öğrenim gördüğünüz dal): _____
İşiniz (Halen yapmakta olduğunuz iş): _____
☐ Memur / Bürokrat (Açıklayınız): _____
☐ İşçi (Açıklayınız): _____
☐ Serbest meslek (Açıklayınız): _____
☐ Öğrenci ☐ İşsiz ☐ Emekli, çalışmıyor ☐ Ev hanımı

- **Daha önce çalışmış olduğunuz iş kollarını belirtiniz (5'ten fazlaysa, en uzun çalıştığınız 5'ini yazınız):**

1) İş kolu: _____ Görev: _____ İşe başlama yılı: ____ Çalışma süresi: __ yıl
2) İş kolu: _____ Görev: _____ İşe başlama yılı: ____ Çalışma süresi: __ yıl
3) İş kolu: _____ Görev: _____ İşe başlama yılı: ____ Çalışma süresi: __ yıl
4) İş kolu: _____ Görev: _____ İşe başlama yılı: ____ Çalışma süresi: __ yıl
5) İş kolu: _____ Görev: _____ İşe başlama yılı: ____ Çalışma süresi: __ yıl

- **Öğrenim durumunuz nedir?**

☐ Okur-yazar değil ☐ Sadece okur-yazar ☐ İlkokul mezunu
☐ Ortaokul mezunu ☐ Lise mezunu ☐ Üniversite mezunu
☐ Yüksek lisans (Master) ☐ Doktora

- **Halen yaşadığınız eve giren toplam aylık gelir ne kadardır?**

☐ 500 YTL'den az ☐ 500-1000 YTL arası ☐ 1000-3000 YTL arası
☐ 3000 YTL'den çok

- **Sosyal güvenceniz nedir? (Sağlık masraflarınızı hangi kurum karşılıyor?)**

☐ Emekli Sandığı ☐ SSK ☐ Bağ-Kur
☐ Özel sigorta (Belirtiniz): _____
☐ Diğer (Belirtiniz): _____

B - Kişisel Öykü

Doğal saç renginiz: ☐ Siyah ☐ Kumral ☐ Sarı ☐ Kızıl ☐ Diğer (Belirtiniz):
Göz renginiz: ☐ Siyah ☐ Kahverengi ☐ Yeşil ☐ Mavi ☐ Diğer (Belirtiniz):
Cilt renginiz: ☐ Buğday ☐ Buğdaydan açık ☐ Buğdaydan koyu

- **Size daha önce kanser teşhisi konuldu mu?**

☐ Hayır ☐ Evet

Evet ise:
1. Kanser tipi: Tanı yaşı: _____

Halen kansere yönelik tedavi alıyor musunuz?
☐ Hayır ☐ Evet (belirtiniz): _____
2. Kanser tipi: _____ Tanı yaşı:

Halen kansere yönelik tedavi alıyor musunuz?
☐ Hayır ☐ Evet (belirtiniz): _____

- **Daha önce vücudunuzun herhangi bir yerinden ben (nevüs) aldırdınız mı?**

☐ Evet ☐ Hayır

- **Aldırdınız ise patolojik tanınız neydi?**

☐ Melanositik, displastik veya atipik nevüs 0 Diğer (Belirtiniz): _____

- **Daha önce sedef veya diğer deri rahatsızlıkları için PUVA tedavisi aldınız mı?**

☐ Evet ☐ Hayır

- **Çocukken ciddi güneş yanığı geçirdiniz mi?**
  ☐ Evet, sık sık ☐ Evet, bazen ☐ Hayır

- **Bronzlaşmak amacıyla solaryum vb. cihazları kullanır mısınız?**
  ☐ Evet, sık sık ☐ Evet, bazen ☐ Hayır

C - Hastalık ve İlaç Öyküsü

Bir doktor tarafından teşhis edilmiş önemli hastalıklar veya geçirdiğiniz ameliyatları belirtiniz:

• Hastalık	Teşhis yaşı	Uygulanan Tedaviler
☐ Hipertansiyon	_____	_____
☐ Diabet (Şeker hastalığı)	_____	_____
☐ Osteoporoz	_____	_____
☐ Crohn hastalığı	_____	_____
☐ Ülseratif kolit	_____	_____
☐ Kolorektal adenom (Kalın barsakta polip)	_____	_____

- **Diğer hastalık / ameliyatlar:**
  ☐ _____ _____
  ☐ _____ _____
  ☐ _____ _____
  ☐ _____ _____

- **Düzenli aspirin kullanır mısınız?**
  ☐ Hayır
  ☐ Evet, ____ yıldır, günde ____ mg (Dozunu bilmiyorsanız preparat adını yazınız: _____)
  Diğer ağrı kesiciler: 1) _____; haftada _____ tablet
  2) _____; haftada _____ tablet
  3) _____; haftada _____ tablet

- **Hemen her gün düzenli olarak kullandığınız ilaç var mı? (Vitamin vb. ilaçları da yazınız)**

İlaç	Süre	İlaç	Süre
1) _____	_____	5) _____	_____
2) _____	_____	6) _____	_____
3) _____	_____	7) _____	_____
4) _____	_____	8) _____	_____

D - Aile Öyküsü

- **Yakın akrabalarınızda (anne, baba, kardeş, çocuk ve eş) kanser tanısı konulmuş olan kimse var mı?**
  ☐ Yok ☐ Var

  Var ise yakınlık derecesi:

1) _____	Kanser tipi: _____	Yaklaşık tanı yaşı: _____
2) _____	Kanser tipi: _____	Yaklaşık tanı yaşı: _____
3) _____	Kanser tipi: _____	Yaklaşık tanı yaşı: _____
4) _____	Kanser tipi: _____	Yaklaşık tanı yaşı: _____

E - Alışkanlıklar

- **Alkol** ☐ Hiç kullanmam. ☐ Kullanırım.
- **Bira** : Yaklaşık ____ günde bir, ____ büyük şişe (500 cc); ____ yıl süreyle
- **Şarap** : Yaklaşık ____ günde bir, ____ kadeh (50 cc); ____ yıl süreyle
- **Rakı** : Yaklaşık ____ günde bir, ____ duble (80 cc); ____ yıl süreyle
- **Diğer (Belirtiniz):** _____ haftada yaklaşık ____ kadeh; ____ yıl süreyle

- **Türk kahvesi** : Haftada yaklaşık ____ kahve fincanı
- **Neskafe** : Haftada yaklaşık ____ büyük fincan
- **Çay** : Haftada yaklaşık ____ çay bardağı
- **Sigara** ____ yıldır günde ____ adet içiyorum.
  ____ yıl günde ____ adet içtim, ____ yıl önce bıraktım.
  ☐ Hiç içmedim.

- **Hiç sigara içmediyseniz, sigara içen biriyle aynı evde yaşadınız mı?**
  ☐ Hayır
  ☐ Evet, çocukluğumda
  ☐ Evet, erişkin çağda
  ☐ Evet, hem çocukluğumda, hem de erişkin çağda

- **Hiç sigara içmediyseniz, günde yaklaşık kaç saatinizi sigara içilen bir ortamda geçiriyorsunuz?** ___ saat

- **Yaklaşık ne kadar televizyon seyredersiniz?**
  ☐ Hemen hiç seyretmem.
  ☐ Günde ortalama ____ saat seyrederim.

- **Düzenli olarak cep telefonu kullanır mısınız?**
  ☐ Hayır, hiç kullanmadım.
  ☐ Nadiren kullanırım (Haftada en fazla birkaç kez, birkaç dakika süreyle)
  ☐ Evet, ____ yıldır kullanıyorum. Günde yaklaşık ____ kez, her seferinde ____ dakika konuşurum.

F - Fiziksel Aktivite

- **İşinizi yaparken ne kadar güç harcarsınız?**
  ☐ İşimi yaparken hiç terlemem (Masa başı görevler vb.) (Hareketsiz).
  ☐ İşimi yaparken bazen terleyecek kadar güç harcamam gerekir (Orta derecede hareketli).
  ☐ İşimi yaparken güç harcarım ve terlerim (Bedensel güce dayalı).

- **Spor yapar mısınız?**
  ☐ Amatör/profesyonel sporcuyum, belirli aralıklarla yarışma/maçlara katılırım; haftada ____ kez, her seferinde yaklaşık ____ dakika süreyle
  ☐ Düzenli spor yaparım; haftada ___ kez, her seferinde yaklaşık ___ dakika süreyle
  ☐ Arada spor yaparım; ayda ___ kez, her seferinde yaklaşık ___ dakika süreyle
  ☐ Nadiren (ayda birden daha az) spor amaçlı egzersiz yaparım.
  ☐ Spor yapmam.

Yaptığınız spor cinsini belirtiniz.
_____
_____
_____
_____

G - Beslenme Alışkanlıkları

- **Ne sıklıkta ve miktarda kırmızı et tüketirsiniz?**
  ☐ Vejeteryanım, hiç et yemem.
  ☐ Haftada bir porsiyon veya daha nadir
  ☐ Haftada 2-3 porsiyon
  ☐ Haftada 3 porsiyondan fazla

- **Ne sıklıkta ve miktarda taze sebze ve meyve tüketirsiniz?**
  (Örneğin orta büyüklükte bir elma veya şeftali veya 3 kayısı veya 12 üzüm bir porsiyon kabul edilmektedir.)
  ☐ Günde bir porsiyondan az
  ☐ Günde 1-2 porsiyon
  ☐ Günde 3 porsiyon veya daha fazla

- **Tuzlanarak veya tütsülenerek kurutulmuş gıdaları (pastırma, füme balık ve peynirler vb.) hangi sıklıkta tüketirsiniz?**
  - ☐ Hemen her gün
  - ☐ Haftada 2-3 kez
  - ☐ Haftada ortalama bir kez
  - ☐ Ayda 1-2 kez
  - ☐ Birkaç ayda bir veya hiç

BU BÖLÜM SADECE ERKEKLER TARAFINDAN DOLDURULACAKTIR. BAYANLARIN BİR SONRAKI SAYFADAKI BÖLÜMÜ DOLDURMALARI GEREKMEKTEDİR.

H1 - Üreme Sağlığı

- **Hayatınızının herhangi bir döneminde PSA (Prostat Spesifik Antijen) testi yaptırdınız mı?**
  - ☐ PSA'nın ne olduğunu bilmiyorum.
  - ☐ Hayır, hiç yaptırmadım, yaptırmayı planlamıyorum.
  - ☐ Hayır, hiç yaptırmadım, ancak __/__/__ tarihinde yaptırmayı planlıyorum.
  - ☐ Evet, en son __/__/__ tarihinde yaptırdım, ancak tekrar yaptırmayı planlamıyorum.
  - ☐ Evet, en son __/__/__tarihinde yaptırdım, __/__/__ tarihinde tekrar yaptırmayı planlıyorum.

- **Daha önce (rekto)sigmoidoskopi yaptırdınız mı?**
  - ☐ Rektosigmoidoskopinin ne olduğunu bilmiyorum.
  - ☐ Hayır, hiç yaptırmadım, yaptırmayı planlamıyorum.
  - ☐ Hayır, hiç yaptırmadım, ancak __/__/__ tarihinde yaptırmayı planlıyorum.
  - ☐ Evet, en son __/__/__ tarihinde yaptırdım, ancak tekrar yaptırmayı planlamıyorum.
  - ☐ Evet, en son __/__/__ tarihinde yaptırdım, __/__/__ tarihinde tekrar yaptırmayı planlıyorum.

- **Daha önce gaitada (dışkıda) gizli kan testi yaptırdınız mı?**
  - ☐ Gaitada gizli kan testinin ne olduğunu bilmiyorum.
  - ☐ Hayır, hiç yaptırmadım, yaptırmayı planlamıyorum.
  - ☐ Hayır, hiç yaptırmadım, ancak __/__/__ tarihinde yaptırmayı planlıyorum.
  - ☐ Evet, en son __/__/__ tarihinde yaptırdım, ancak tekrar yaptırmayı planlamıyorum.
  - ☐ Evet, en son __/__/__ tarihinde yaptırdım, __/__/__ tarihinde tekrar yaptırmayı planlıyorum.

Anket bitmiştir. Ayırdığınız zaman ve verdiğiniz bilgiler için teşekkür ederiz.

SADECE BAYANLAR TARAFINDAN DOLDURULACAKTIR.

H2 - Üreme Sağlığı

İlk adet yaşınız: ___ ☐ Hiç adet görmedim.

- **Halen adet görüyor musunuz?**
  - ☐ Hayır, ___ yıl önce kesildi.
  - ☐ Evet, düzenli olarak ___ günde bir.
  - ☐ Evet, ancak uzun süredir düzensiz.
  - ☐ Evet, ancak yakın zamanda düzensizleşti.
- **Düzensizliğin muhtemel nedeni:**
  - ☐ Menopoz
  - ☐ Başka (Açıklayınız): _____
  - ☐ Bilmiyorum
- **Adetten kesildiyseniz, hormon replasman tedavisi (menopoz sonrası hormon tedavisi) kullandınız mı?**
  - ☐ Hiç kullanmadım.
  - ☐ Evet, ___ yıldır kullanıyorum.
  - ☐ Evet, ___ yıl süreyle kullandım, ___ yıl önce bıraktım.
- **Hiç gebe kaldınız mı?**
  - ☐ Hayır ☐ Evet

  Evet ise (Uymayanları boş bırakınız):

  İlk bebeğinizi doğurduğunuz yaş: ___

  Toplam doğum sayısı: ___

  Doğurduğunuz canlı bebek sayısı: ___

  Düşük sayısı: ___

  Kürtaj sayısı: ___
- **Bebek emzirdiniz mi?**
  - ☐ Hayır ☐ Evet, toplam ___ ay süreyle (birden fazla çocuğunuzu emzirdiyseniz toplam emzirme süresini yazınız.)
- **Doğum kontrol hapı kullandınız mı?**
  - ☐ Hiç kullanmadım.
  - ☐ Evet, ___ yıldır kullanıyorum.
  - ☐ Evet, ___ yıl süreyle kullandım, ___ yıl önce bıraktım.
- **Hiç tamoksifen / raloksifen (Evista ®) adlı ilaçları kullandınız mı?**
  - ☐ Hiç kullanmadım.
  - ☐ Evet, ___ yıldır kullanıyorum.
  - ☐ Evet, ___ yıl süreyle kullandım, ___ yıl önce bıraktım.

İlk koitus (cinsel ilişki) yaşınız: ___

Bugüne kadar cinsel partner (cinsel eş) sayınız: ___

- **Sizin veya eşinizin birden fazla cinsel eşinin bulunması serviks kanseri açısından riskli bir durumdur. Bu açıdan risk taşıyor olabilir misiniz?**
  - ☐ Evet
  - ☐ Hayır
  - ☐ Emin değilim.

- **Size cinsel yolla bulaşan bir hastalık teşhisi konuldu mu?**
  ☐ Hayır ☐ Evet, konulan tanı _____ idi.
  ☐ Evet, ancak teşhisi hatırlamıyorum.

  Eşinize/partnerinize cinsel yolla bulaşan bir hastalık teşhisi konuldu mu?
  ☐ Evet, konulan tanı _____ idi. ☐ Hayır
  ☐ Evet, ancak teşhisi hatırlamıyorum.

- **Cinsel ilişki esnasında hangi sıklıkta kondom (prezervatif) kullanırsınız?**
  ☐ Hiçbir zaman
  ☐ Ara sıra
  ☐ Sıklıkla
  ☐ Her zaman

- **Memenizden parça alındı mı?**
  ☐ Hayır, hiç alınmadı.
  ☐ Evet, __ kez alındı, ancak sonucunu tam bilmiyorum.
  ☐ Evet, __ kez alındı ve sonucu iyi huylu bulundu (Aşağıdakilerden uygun olanı işaretleyiniz).
  ☐ Fibroadenom ☐ Fibrokistik hastalık ☐ Atipik hiperplazi
  ☐ Diğer: _____
  ☐ Evet, alındı ve kötü huylu bulundu. Açıklayınız: _____

- **Göğüs bölgenize ışın tedavisi aldınız mı?**
  ☐ Hayır.
  ☐ Evet, _____ nedeniyle.

- **Yumurtalıklarınız (overler) ameliyatla alındı mı?**
  ☐ Hayır.
  ☐ Evet, biri _____ nedeniyle, _____ yılında alındı.
  ☐ Evet, ikisi de _____ nedeniyle, _____ yıl(lar)ında alındı.

- **Memeniz ameliyatla alındı mı?**
  ☐ Hayır.
  ☐ Evet, biri _____ nedeniyle, ____ yılında alındı.
  ☐ Evet, ikisi de _____ nedeniyle, ____ yıl(lar)ında alındı.

- **Daha önce mamografi yaptırdınız mı?**
  ☐ Mamografinin ne olduğunu bilmiyorum.
  ☐ Hayır, hiç yaptırmadım, yaptırmayı planlamıyorum.
  ☐ Hayır, hiç yaptırmadım, ancak __ /__ /__ tarihinde yaptırmayı planlıyorum.
  ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, ancak tekrar yaptırmayı planlamıyorum.
  ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, __ /__ /__ tarihinde tekrar yaptırmayı planlıyorum.

- **Daha önce (rekto)sigmoidoskopi yaptırdınız mı?**
  ☐ Rektosigmoidoskopinin ne olduğunu bilmiyorum.
  ☐ Hayır, hiç yaptırmadım, yaptırmayı planlamıyorum.
  ☐ Hayır, hiç yaptırmadım, ancak __ /__ /__ tarihinde yaptırmayı planlıyorum.
  ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, ancak tekrar yaptırmayı planlamıyorum.
  ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, __ /__ /__ tarihinde tekrar yaptırmayı planlıyorum.

- **Daha önce gaitada (dışkıda) gizli kan testi yaptırdınız mı?**
  - ☐ Gaitada gizli kan testinin ne olduğunu bilmiyorum.
  - ☐ Hayır, hiç yaptırmadım, yaptırmayı planlamıyorum.
  - ☐ Hayır, hiç yaptırmadım, ancak __ /__ /__ tarihinde yaptırmayı planlıyorum.
  - ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, ancak tekrar yaptırmayı planlamıyorum.
  - ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, __ /__ /__ tarihinde tekrar yaptırmayı planlıyorum.

- **Daha önce Pap smear (smir) testi (rahim ağzı sürüntüsü) yaptırdınız mı?**
  - ☐ Pap smear testinin ne olduğunu bilmiyorum.
  - ☐ Hayır, hiç yaptırmadım, yaptırmayı planlamıyorum.
  - ☐ Hayır, hiç yaptırmadım, ancak __ /__ /__ tarihinde yaptırmayı planlıyorum.
  - ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, ancak tekrar yaptırmayı planlamıyorum.
  - ☐ Evet, en son __ /__ /__ tarihinde yaptırdım, __ /__ /__ tarihinde tekrar yaptırmayı planlıyorum.

Anket bitmiştir. Ayırdığınız zaman ve verdiğiniz bilgiler için teşekkür ederiz.

Appendix 2. Ethics Committee Approval Letter

T.C.
HACETTEPE ÜNİVERSİTESİ
Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu

Sayı : 16969557 — 104

24 Ocak 2014

ARAŞTIRMA PROJESİ DEĞERLENDİRME RAPORU

Toplantı Tarihi : 22.01.2014 ÇARŞAMBA
Toplantı No : 2014/02
Proje No : GO 14/ 04 (Değerlendirme Tarihi 08.01.2014)
Karar No : GO 14/ 04 - 06

Üniversitemiz Kanser Enstitüsü Prevantif Onkoloji Anabilim Dalı öğretim üyelerinden Doç.Dr.Saadettin KILIÇKAP'ın sorumlu araştırmacısı olduğu Dr.Nooria ATTA'nın tezi olan GO 14/04 kayıt numaralı ve ***"Hacettepe Üniversitesi Onkoloji Hastanesinde Tedavi Alan Kanser Hastalarının Yakınları Arasında Jinekolojik Kanser Risk Faktörleri"*** başlıklı proje önerisi araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş olup, etik açıdan uygun bulunmuştur.

1.Prof. Dr. Nurten Akarsu	(Başkan)	9 Prof. Dr. Melahat Görduysus	(Üye)
İZİNLİ			
2. Prof. Dr. Nüket Örnek Buken	(Üye)	10. Prof. Dr. Cansın Saçkesen	(Üye)
3. Prof. Dr. M. Yıldırım Sara	(Üye)	11. Prof. Dr. R. Köksal Özgül	(Üye)
4. Prof. Dr. Sevda F. Müftüoğlu	(Üye)	12. Prof. Dr. Ayşe Lale Doğan	(Üye)
5. Prof. Dr. Cenk Sökmensüer	(Üye)	13 Doç. Dr. S. Kutay Demirkan	(Üye)
İZİNLİ			
6. Prof. Dr. Volga Bayrakçı Tunay	(Üye)	14. Prof. Dr Leyla Dinç	(Üye)
7. Prof. Dr. Songül Vaizoğlu	(Üye)	15. Yrd. Doç. Dr. H. Hüsrev Turnagöl	(Üye)
İZİNLİ			
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