

RESEARCH COMMUNICATION

Patho-epidemiology of Cancer Corpus Uteri in Karachi South '1995-1997'

Yasmin Bhurgri^{1,2*}, Kauser Nazir³, Yasmeen Shaheen¹, Ahmed Usman⁴, Naveen Faridi⁵, Hadi Bhurgri^{1,2}, Jawaid Malik^{6,7}, Imtiaz Bashir⁸, Asif Bhurgri^{1, 9, 10, 11}, Sheema H Hasan², Naila Kayani², SHM Zaidi¹²

Abstract

Aim: To provide demographics and pathology of cancer of the uterine corpus in Karachi. **Methodology:** Data for 66 incident cases of cancer corpus uteri, ICD-10 category C54-5 registered at the Karachi Cancer Registry, for Karachi South, during a 3 year period, 1st January, 1995 to 31st December 1997 were reviewed. **Results:** Cancer uterine corpus (1995-97) was the sixth most common malignancy, following breast, oral cavity, ovary, esophagus and cervix. The age standardized incidence rate (ASR) world and crude incidence rate (CIR) per 100,000 were 6.4 (4.73 to 8.01) and 2.9 (2.18 to 3.57). The mean age was 53.7 years (SD 15.6; range 6-90 years). Fifty eight cases were endometrial carcinoma with ASR world and CIR per 100,000 of 5.77 (4.20 to 7.33) and 2.53 (1.88 to 3.18) respectively. Sarcomas comprised 6% of the cases. Approximately a third of the females (28.8%) were below 50 years of age. The age-specific curves showed a gradual increase from the fourth till the seventh decade, followed by an actual apparent decrease in risk after 70 years. Peak incidence was observed in the 65-69 year age group. Presenting symptoms were post-menopausal bleeding (86.4%) and purulent discharge (4%). Associated pathologies included adenomyosis, adenomatous hyperplasia (12% each) or leiomyoma (8%). Associated clinical conditions were diabetes mellitus and hypertension (4% each). The majority of the cases presented as well differentiated (39.4%), localized (59.1%) lesions. **Conclusion:** The incidence of cancer corpus uteri in Karachi South reflects a moderate risk population, predominantly middle aged with a higher socio-economic status. On the average the malignancy is observed a decade earlier then reported elsewhere. This calls for in-depth investigation of risk factors and identification of underlying etiology.

Key Words: Corpus uteri - cancer - Karachi - Pakistan

Asian Pacific J Cancer Prev, 8, 489-494

Introduction

Cancer of the corpus uteri ICD-10 category C54 (International Classification of Diseases 10th Revision), is the most common pelvic gynecologic malignancy in most developed countries (Djordjevi and Stanojevi, 2007). Approximately 39,000 cases of corpus cancer were predicted to occur in the United States in 2007, making it the fourth most common cancer among women; of these women, approximately 7400 are expected to die from the disease (Creasman and Sims, 2007). In developing countries of Asia, with the possible exception of the Muslim countries, cancer cervix still occupies either the top rank amongst gynecologic malignancies or the top rank amongst all female cancers (Moore M and Tajima K, 2004). A wide variation is observed in the global incidence of uterine cancer. In the eighth volume of 'Cancer Incidence in the Five Continents' (CIV-VIII) the

age-standardized incidence rates (ASRs per 100,000 population) for cancer uterine corpus for the years 1993-97, all ages included, varied from the lowest (0.5) in Oman to the highest (26.6) in US, Hawaii (Parkin, et al 2002).

Approximately 95% of uterine malignancies are endometrial carcinoma and 4% are sarcomas. Endometrial carcinoma is not a single entity. Differences in the epidemiology, risk factors, morphology and biological behavior suggest two pathogenetic groups. Type I or the endometrioid type represents two thirds of the cases, commonly occurs in pre and peri-menopausal women, with an associated history of unopposed estrogen exposure and/or hyperlipidemia and obesity. Signs of hyperestrogenism include anovulatory uterine bleeding, infertility, late onset of menopause, ovarian stromal hyperplasia, and endometrial hyperplasia. These tumours are low grade, minimally invasive and associated with a good prognosis. Type II, the non-endometrioid type,

¹Karachi Cancer Registry ²Aga Khan University, Pathology ³Lady Dufferin Hospital ⁴Jinnah Postgraduate Medical Centre, Radiotherapy ⁵Liaquat National Hospital, Pathology ⁶Liaquat National Hospital, Oncology ⁷Ziauddin Hospital, Oncology ⁸Zainab Punjwani Hospital, Oncology ⁹Zainab Punjwani Hospital, Pathology ¹⁰Sindlab, Karachi ¹¹Anklesaria Nursing Home ¹²Baqai Institute of Oncology *Corresponding author: Pathology & Microbiology Department, Agakhan University, Stadium Road, P.O. Box 3500, Karachi 74800, Pakistan. Fax: 92 21 493 4294, 493 2095 Email: bhurgri@cyber.net.pk

comprise the more aggressive high-grade papillary serous and clear cell endometrial carcinoma. These cancers occur in older, post-menopausal women, are more common in African-Americans and unassociated with hyperestrogenism. Atypical hyperplasia is recognized as the precursor for the endometrioid carcinoma and endometrial intraepithelial carcinoma (EIC) the precursor of serous carcinoma (Djordjevi and Stanojevi, 2007).

In the endometrioid type of endometrial carcinoma, PTEN mutation may be central to the initiation of endometrial proliferative lesions by which damage in other genes is then accumulated (e.g. DNA mismatch repair genes, K-ras, p53) in the progression to carcinoma. In contrast p53 mutations appear to be important in the conversion of atrophic endometrium to serous adenocarcinoma (Djordjevi and Stanojevi, 2007). Uterine sarcoma include carcinosarcoma or mixed homologous müllerian tumors (48-50%), leiomyosarcoma (LMS; 38-40%), endometrial stromal sarcoma (EES; 8-10%) and rarely rhabdomyosarcoma, osteosarcoma, and chondrosarcoma (Winter WE and Gosewehr JA, 2006).

Pakistan is an Islamic Republic in Southern Asia, bordering the Arabian Sea (30 00 N, 70 00 E). It is situated between India on the east, Iran and Afghanistan on the west and China in the north. Largely an agricultural country it is divided into 4 administrative divisions or provinces (Sindh, Punjab, Baluchistan and North-West Frontier Province), a territory (Federally Administered Tribal Areas), a capital territory (Islamabad), and the Pakistani-administered portion of the disputed Jammu and Kashmir region (Azad Kashmir and the Northern Areas). The major ethnic groups in the country are Punjabi, Sindhi, Pashtun (Pathan), Baloch, Muhajir (immigrants from India at the time of partition and their descendants). Muslims comprise 97% of the population with the Christians, Hindus, and other religions comprising 3% of the population. Pakistan is a developing country, which falls into the low to medium resource category by WHO classification (The World Factbook, 2007; World Health Report 2007).

Karachi South (KS) is the southern-most, all urban, district of Karachi, which forms a belt along the Arabian Sea. It has a strong western influence. The hierarchy of malignancies in Karachi (age standardized incidence rate per 100,000) for the years 1995-97 was breast cancer ICD-10 categories C50 (53.1), oral cavity ICD-10 categories C00-08 (15.5), ovary ICD-10 category C56 (10.9), esophagus ICD-10 category C15 (6.9), cervix ICD-10 category C53 (6.8), uterus ICD-10 categories C54 (6.4),

colo-rectum ICD-10 categories C18-20 (5.5), gall bladder ICD-10 category C23 (5.3), skin ICD-10 category C44 (4.9), lymphoma ICD-10 categories C81-85; C96 (4.4); and thyroid ICD-10 category C73 (4.2) (Bhurgri et al, 2002).

The present study was conducted with the objective of examining descriptive epidemiological and pathological characteristics of cancer corpus uteri in Karachi South.

Methodology

Epidemiological data of incident cancer corpus uteri, ICD-10 category C54 registered at KCR for Karachi South, during 1st January 1995 to 31st December 1997 were reviewed. The study included clinically diagnosed and microscopically verified malignancies of corpus uteri. All surgical specimens were initially evaluated on hematoxylin and eosin (H&E) stained sections. Special stains were selectively used, whenever required.

The reported epidemiological cancer data were rechecked, and residency status re-ascertained. People residing in the specified geographical regions for more than six months were considered residents. The cases were categorized by tumor site, age and sex of the patient. Variables recorded were the hospital patient-number, date of incidence, name, age, sex, address, ethnicity, topography, morphology, grading and staging (TNM). The data were classified using ICD-O3 (International Classification of Diseases-Oncology, 3rd edition) and computerized using a customized version of CANREG-4 software. This software includes facilities for the detection of duplicate registrations and for performing internal checks on the validity of the entered data. Manual and computerized validity check for the cancer data were performed as per recommendations of International Agency for Research on Cancer (IARC) and International Association of Cancer Registries (IACR) (Parkin et al, 1994).

Crude, age-standardized, and age-specific incidence rates (CIR, ASR, ASIR) were calculated. The person-years of female population at risk by 5-year age-groups were estimated with the mid 1996 population, estimates based on the 1998 census, copy obtained from the Sindh Bureau of Statistics, total population of 1,724,915; females 795,521, assuming an annual growth rate of 1.94%. The growth rates were based on the inter-census growth-rate and measures for inflow and outflow of population, calculated by the Federal Bureau of Statistics. Standardized incidence rate was calculated with an external reference

Table 1. South Karachi (1995-97), Incidence Rates/100,000 for Corpus Uteri, All Ages, by Site and Morphology

Site	Crude rate (95% CI)	ASR-World (95% CI)	ASR-European (95% CI)	Total Cases
Female genital organs	12.90 (11.5 to 14.4)	25.50 (22.4 to 28.6)	33.35 (29.1 to 37.6)	297
Corpus uteri	2.88 (2.18 to 3.57)	6.37 (4.73 to 8.01)	8.64 (6.40 to 10.9)	66
Morphology				
Adenocarcinoma	2.53 (1.88 to 3.18)	5.77 (4.20 to 7.33)	7.91 (5.76 to 10.1)	58
Other carcinoma	0.09 (-0.03 to 0.21)	0.17 (-0.08 to 0.42)	0.21 (-0.10 to 0.51)	2
Unspecified carcinoma	0.09 (-0.03 to 0.21)	0.21 (-0.12 to 0.55)	0.27 (-0.17 to 0.72)	1
Sarcoma	0.13 (-0.02 to 0.28)	0.11 (-0.02 to 0.24)	0.11 (-0.03 to 0.24)	3

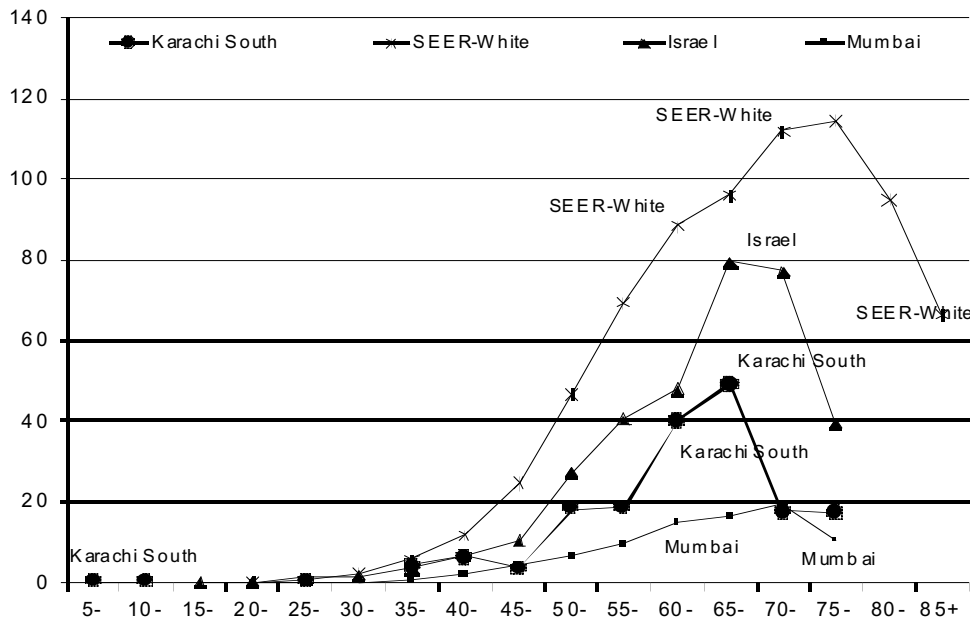


Figure 1. Cancer Corpus Uteri-ASIRs in Karachi South(KS) in Comparison to Contemporary Asian Registries and SEER White. The ASIRs for KS are lower than Israel and US SEER for all age groups except the childhood groups. The KS ASIRs remain higher than the incidence rates of Bombay for all groups.

population, the ‘world’ population with a given ‘standard’ age distribution (Segi, 1960). ‘The standardized rate is the incidence rate that, theoretically, would have been observed if the population had a standard age distribution. The methodology applied was direct standardization, using 5-year age groups. The rates given are the annual incidence per 100,000 population averaged over the number of years for which data are presented’. Incidence tables were based on ICD-10 (WHO, 1992).

To determine the socioeconomic profile, the district was divided into 3 subcategories based on the income of approximately 70% of the resident population. The categories ranged from 1 to 3 in an ascending income strata (table 1). Category I was composed of the predominantly financially deprived class with an annual income of less than \$2000, and a low literacy level. Residents of category II had an annual income range of \$2001-\$20,000 with a moderately high literacy. Category III was largely made up of educated professionals, with

an annual income of more than \$20,000. A sample survey was conducted to categorize the financial status of the population. The data were analyzed using SPSS 15.0.

Results

A total of 66 cases of cancer corpus uteri ICD-10 (International Classification of Diseases 10th Revision) category C54-5 were registered at the Karachi Cancer Registry, for Karachi South, during a 3 year period, 1st January, 1995 to 31st December 1997. The age standardized incidence rate (ASIR) world and crude incidence rate (CIR) per 100,000 were 6.4 (4.73 to 8.01) and 2.9 (2.18 to 3.57). The incidence for different morphologies is given in table 1.

Three cases (4.6%) were observed in the pediatric age group ≤14 years. Six (9.1%) cases were observed in women between 15 and 40 years of age. Approximately a third of the females (28.8%) were below 50 years of age.

Table 2. Pakistan, South Karachi (1995-97), Mean Age, Range Standard Deviation by Site and Morphology

Site	Frequency # (%)	Mean Age (95% CI)	Range	Standard Deviation
Corpus uteri	66	53.7 (53.7; 49.9)	6-90	15.6
Morphology				
Carcinoma	61 (92.4)	56.0 (52.9; 59.2)	25-90	12.4
-Adenocarcinoma, nos	52 (78.8)	56.7 (53.3; 60.1)	25-90	12.2
-Papillary adenocarcinoma	3 (4.5)	58.3 (14.7; 101)	40-75	17.6
-Endometroid adenocarcinoma	3 (4.5)	54 (28.2; 79.8)	42-60	10.4
-Squamous cell carcinoma	1 (1.5)	40	-	-
-Unspecified carcinoma	1 (1.5)	35	-	-
Sarcoma	3 (4.6)	29.8 (-9.9; 69.4)	6-60	24.9
-Rhabdomyosarcoma	2 (3.0)	9.5 (-34.9; 53.9)	6 & 13	4.9
-Leiomyosarcoma	1 (1.5)	40	-	-
Other morphology	2 (3.0)			
-Endometrial stromal sarcoma	1 (1.5)	60	-	-
-Mixed mesodermal tumour	1 (1.5)	7	-	-

The age-specific curves showed a gradual increase from the fourth up till the seventh decade, followed by an actual apparent decrease in risk after 70 years of age (Figure 1). The peak incidence was observed in the 65-69 year age group.

Microscopic confirmation of malignancies was 100%. The morphological categorization was adenocarcinoma (ICD 10 category M8140-3) 52 cases (78.8%), papillary adenocarcinoma (ICD 10 category M8260-3) and endometrioid carcinoma (ICD 10 category M8380-3) 3 cases (4.5%) each. Squamous cell carcinoma (ICD 10 category M8070-3) comprised 1 case (1.5%) and carcinoma not otherwise specified - NOS (ICD 10 category M8010-3) 2 cases (3.0%). Thus carcinomas were observed in 92.4% cases.

A total of 58 cases of endometrial carcinoma were registered, the ASR world and CIR per 100,000 were 5.77 (4.20 to 7.33) and 2.53 (1.88 to 3.18) respectively. Four cases of sarcoma, ASR world 0.11 (-0.02 to 0.24) and CIR 0.13 (-0.02 to 0.28) were also registered. Sarcomas comprised 6% cases. The subcategories of sarcoma were rhabdomyosarcoma (ICD 10 category M8900-3) 2 cases (3.0%), leiomyosarcoma (ICD 10 category M8890-3) and endometrial stromal sarcoma (ICD 10 category M8930-3), 1 case (1.5%) each.

The mean age of the cancer cases was 53.7 years (SD 15.6; 95% CI 53.7, 49.9; range 6-90 years). The mean age of endometrial carcinoma cases was 56.7 years (SD 12.2; 95% CI 53.3, 60.1, range 25-90 years). The mean ages of different morphologies are given in table 2. The only case of leiomyosarcoma (M8890-3) was observed in a 40 year old female, rhabdomyosarcoma (M8900-3) in 2 females, 6 and 13 years of age, endometrial stromal sarcoma (M8930-3) in a 60 year old female and mesodermal mixed tumour (M8951-3) in a 7 year old child.

The distribution by religion was Muslims (64 cases; 97.0%) and Christians (2 cases; 3.0%). There were no cases reported in Hindus or Parsees. The frequency distribution by ethnicity was Urdu speaking Mohajirs (17 cases; 25.8%), Punjabis (7 cases; 10.6%), Gujrati speaking Mohajirs (6 cases; 9.1%), memon Mohajirs (6 cases; 9.1%), Sindhis (5 cases; 7.6%), Pathans (3 cases; 4.5%) and Baluchs (1 case; 1.5%). The ethnicity was not known in 21 cases (31.8%).

The socio-economic distribution was 11 cases (16.7%) in category I the financially deprived class, 22 cases (33.3%) in category II the middle class and 33 cases (50.0%) in category III, the upper middle and affluent class. There were 49 (74.2%) married women, 4 (6.1%) unmarried women and 8 (12.1%) widows. The marital status was not known for 5 (7.6%) cases (table 2). Housewives formed the bulk of the cases (62 cases, 93.9%), whereas there was 1 (1.5%) professionally working woman, a teacher and 3 (4.5%) unskilled workers.

The predominant presenting symptom was post-menopausal bleeding which was observed in 57 (86.4%) cases and purulent discharge in 4% of the patients. Associated pathologies included adenomyosis and adenomatous hyperplasia in 12% each and leiomyoma uterus in 8%. The associated clinical conditions observed

were diabetes mellitus and hypertension (4% each). History was not available in approximately 10% of the cases.

Majority of the cases presented as well differentiated or grade 1 lesions (26 cases; 39.4%). There were 25 (37.9%) moderately differentiated or grade 2 lesions and 12 (18.2%) poorly differentiated (grade 3) malignancies. The tumor grade was not known in 3 (4.5%) cases.

Localized malignancy was observed in 39 (59.1%) cases. Approximately a fourth of the cancers (18 cases; 27.3%) had spread regionally and 3 (4.5%) cases to a distant site at the time of diagnosis. Six (9.1%) cases could not be staged due to a lack of clinical and pathological information.

Discussion

The incidence of cancer corpus uteri in Karachi South (ASR 6.4 per 100,000) reflects a moderate risk population. The demographic profile of the patients was middle aged women with a higher socio-economic status.

Globocan grades the world region into 5 categories, on a rising scale of 1 to 5 on the basis of the age standardized incidence rates of the country or the estimates of the same prepared by IARC (Ferley et al, 2004). In the first category (grade 1) are included countries with a corpus uteri cancer incidence per 100,000 (ASR/100,000) below 2.3. The other categories are grade 2 (<4.2), grade 3 (<6.9), grade 4 (<12.0) and grade 5 (<22.8). Based on this scheme Pakistan is included in category 3 the moderate risk zone. The incidence of corpus uteri cancer in Karachi South substantiates this categorization. Other populations from Pakistan have reported a lower incidence (ASR per 100,000) viz. Larkana (2.2), Hyderabad (3.4) and Quetta (2.4) albeit with population coverage below optimum completion, indicating a probable higher incidence then reported (Bhurgri et al 2006, Bhurgri et al 2005, and Bhurgri et al 2002). Hospital-based studies in Pakistan have not identified cancer corpus uteri as one of common malignancies in the country (Jamal et al, 2006).

Malignancies of the corpus uteri have a higher incidence in high resource countries. It is the commonest pelvic gynecologic malignancy in most developed countries, whereas in most developing countries it is the third common tumor, after cervix and ovary (Kyari et al, 2004). The moderate risk observed in Karachi is less than the risk for developed countries of North America, Europe and even a few Asian countries but higher than other regional countries. The findings of our study are compatible with a country in socio-economic transition.

Karachi South with an incidence of 6.4/100,000 was the fifth in hierarchy of cancer corpus uteri incidence (ASR/100,000) amongst Asian registries for the 1993-97 period. It was preceded by Jews born in Israel (11.1), Singapore, Chinese (7.9), Singapore, Malay (7.5) and Singapore, Indian (6.9). Comparative contemporary (1993-97) rates in the US for SEER white and for Mumbai were 18.4 and 2.9 per 100,000 respectively (Parkin et al, 2002). In the last 3 decades the white population of the US has retained one of the highest age standardized incidence of endometrial cancer in the world, India and

Japan the lowest, and the European countries have occupied an intermediate position (Cavanagh et al, 1984).

Figure 1 highlights the age specific incidence rates (ASIRs) in Karachi South in comparison to some Asian registries and SEER white (Parkin et al, 2002). The KS ASIRs remain below the rates for Jews in Israel and US SEER white in all age groups. The ASIRs are higher than Mumbai cancer registry till the age of 70 years, thereafter there is an apparent decrease in the risk.

Endometrial carcinoma is primarily a disease of postmenopausal women with a reported mean age at diagnosis of 60 years. Increasing age being a risk factor for endometrial carcinoma, women diagnosed younger than 40 years make up only 5% of the total cases in the United States (Winter and Gosewehr, 2006; Creasman, 2006). In KS 70% of the uterine cancers occurred in women above 50 years, almost half in women 60 years or older, however 15% cancers were observed in women below 40 years, indicating an increased occurrence in younger females. The mean age of the cancer cases in Karachi was 53.7 years which is perimenopausal and nearly a decade younger than observed internationally (Winter and Gosewehr, 2006). Perimenopausal cases are often associated with a history of endometrial hyperplasia, estrogen replacement therapy (ERT), body mass index, diabetes and hypertension. In KS diabetes and hypertension occurred in 4% of the cases and generally Pakistani women have a higher BMI (Jafar et al, 2006). Known protective reproductive factors could not be justified in KS e.g. nearly all (86%) of the women were multiparous. Multiparity appears to be a protective reproductive factor inversely related with the risk of endometrial cancer. Subjects with three or more births have a 70% lower risk than the nulliparous women (Brinton et al, 2007).

The causes of the earlier onset endometrial carcinoma observed in KS need investigation. An increased risk of endometrial carcinoma is also observed in women who have hereditary non-polyposis colon cancer (HNPCC) syndrome. Women with HNPCC account for only 2-10% of all female cases of colon cancer and approximately 5% of all endometrial cancers. These women have a 22-50% lifetime risk of developing endometrial cancer, and the disease tends to occur approximately 15 years earlier (Creasman and Sims, 2007; Horn et al, 2007). This needs further investigation as an earlier onset colonic cancer has also been reported for Karachi (Khurshid et al, 2007). LMS and EES were observed in a 40 year and a 70 year old female respectively. This is compatible with published literature which reports LMS tends to occur more often in women aged 30-50 years and EES in women older than 50 years (Winter and Gosewehr, 2006).

The predominant presenting symptoms of uterine malignancies, both carcinoma and sarcoma in KS were post-menopausal (PMP) bleeding (86.4%) and purulent discharge (4%). PMP bleeding is the most common symptom of women with endometrial cancer, approximately 75% being postmenopausal, (Creasman and Sims, 2007). Endometrial cancer is diagnosed in 12-16% of women with PMP bleeding. Purulent genital discharge is a symptom of advanced disease (Winter and

Gosewehr, 2006). A majority of the patients had associated pathologies indicative of hyper-estrinism which included adenomyosis and adenomatous hyperplasia in 12% each and leiomyoma uterus in 8%. No cases were observed in Parsees, despite an increasing incidence of endometrial carcinoma reported in the community settled in Bombay (Yeole, 1999).

The incidence of uterine cancer in KS and the late stage at presentation, reflect a developing country health-care system with localized malignancy observed in 59.1% of the cancers. In the US, 70-75% of women are diagnosed with surgical stage I disease and though endometrial cancer is the fourth most common cancer in women, following breast, lung, and colorectal cancer, it is the eighth most common cause of cancer death because of early detection (Winter and Gosewehr, 2006).

Conclusions

The incidence of cancer corpus uteri in Karachi South reflects a moderate risk population. In predominantly middle aged women with a higher socio-economic status. On the average the malignancy is observed a decade earlier. This calls for in-depth investigation of risk factors and identification of underlying etiology.

References

- Bhurgri Y, Pervez S, Kayani N, et al (2006). Cancer profile of Larkana 1998-2002. *Asian Pac J Cancer Prev*, **7**, 518-21.
- Bhurgri Y, Bhurgri A, Pervez S, et al (2005). Cancer profile of Hyderabad, Pakistan, 1998-2002. *Asian Pac J Cancer Prev*, **6**, 474-80
- Bhurgri Y, Pervez S, Usman A, et al (2002). Cancer patterns in Quetta (1998-1999). *J Pak Med Assoc*, **52**, 560-5
- Brinton LA, Sakoda LC, Lissowska J, et al (2007). Reproductive risk factors for endometrial cancer among Polish women. *Br J Cancer*, **96**, 1450-6.
- Cavanagh D, Marsden DE, Ruffolo EH (1984). Carcinoma of the endometrium. *Obstet Gynecol Annu*, **13**, 211-60.
- Creasman WT, Sims JM (2007). Endometrial Carcinoma www.emedicine.com/med/topic674.htm; article last updated: 9th Jul, 2007; accessed 6th November 2007
- Djordjevi B, Stanojevi Z (2007). Endometrial carcinoma and precursor lesions. *Srp Arh Celok Lek*, **135**, 230-4.
- Ferlay J, Parkin DM, Pisani P (2004). GLOBOCAN 2002: Cancer incidence, mortality and Prevalence Worldwide IARC CancerBase No. 5, version 2.0, IARC, Lyon.
- Horn LC, Meinel A, Handzel R, et al (2007). Histopathology of endometrial hyperplasia and endometrial carcinoma: an update. *Ann Diagn Pathol*, **11**, 297-311
- Jafar TH, Chaturvedi N, Pappas G (2006). Prevalence of overweight and obesity and their association with hypertension and diabetes mellitus in an Indo-Asian population. *CMAJ*, **175**, 1071-7
- Jamal S, Moghal S, Mamoon N, et al (2006). The pattern of malignant tumours: tumour registry data analysis, AFIP, Rawalpindi, Pakistan (1992-2001). *J Pak Med Assoc*, **56**, 359-62
- Khurshid A, Ahmed R, Bhurgri Y (2007). Primary gastrointestinal malignancies in childhood and adolescence, the Asian perspective. (in press)
- Kyari O, Nggada H, Mairiga A (2004). Malignant tumours of female genital tract in North Eastern Nigeria. *East Afr Med*

- Moore MA, Tajima K (2004). Cervical cancer in the Asian Pacific-epidemiology, screening and treatment. *Asian Pac J Cancer Prev*, **5**, 349-61
- Parkin DM, Chen VW, Ferley J (eds.) (1994). Comparability and Quality Control in Cancer Registration, IARC Technical Report No.19 International Agency for Research on Cancer Lyon.
- Parkin DM, Whelan SL, Ferlay J, et al (2002). Cancer Incidence in Five Continents, Vol. VIII; IARC Scientific Publications No.155 Lyon, France.
- Segi M (1960). Cancer Mortality in Selected Sites -in 24 Countries (1950-57), Sendai, Tohoku University School of Public Health.
- The World Factbook, Pakistan, a country profile (2007), <https://www.cia.gov/library/publications/the-world-factbook/geos/pk.html>, accessed 6th November 2007
- WHO (1992). International Statistical Classification of Diseases and Health Related Problems 10th Revision, Geneva, World Health Organisation.
- World health report (2007). A safer future: global public health security in the 21st century <http://www.who.int/countries/pak/en/>, accessed 6th November 2007
- Winter WE, Gosewehr JA (2006). <http://www.emedicine.com/med/topic2832.htm> Last Updated: May 19, 2006, accessed 6th November 2007.
- Yeole BB, Kurkure A, Advani S, et al (2001). An assessment of cancer incidence patterns in Parsi and Non Parsi populations, Greater Mumbai. *Asian Pac J Cancer Prev*, **2**, 293-8.