Original Article

# Spectrum of Female Genital Tract Cancers in The Pre Covid Verses Covid Pandemic Period at PIMS Pathology Department

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## Abstract

Objective: To determine the trends in gynecological cancers over the past decade, including the latest fifteen months, COVID pandemic period at PIMS.

Methodology: The study was conducted at the Department of Obs & Gynae, MCH Center and Pathology department PIMS, Islamabad from 1st January 2012 to 31st July 2021. Data were entered and analyzed in SPSS version 23.0. Comparison of numbers and rates of different cancers was undertaken for all cases of female genital tract cancers (FGT) in PIMS laboratory during the study. The patient age, histopathology, and immunohistochemistry analyzed. The FGT cancer frequency compared COVID and pre-COVID period. To determine significance, Student t-test and chi-square test have been applied and p value of < 0.05 considered significant.

Results: Total FGT cancer pathologic diagnosis was 168. The annual number of FGT cancer specimens ranged from 13 in 2019 to 22 in 2020. Uterine cancers were 35.1%, cervical 32.7%, ovarian 29.8% while miscellaneous comprised 2.4%. Among the 59 uterine cancers, 53 were endometrioid carcinomas while 6 were stromal tumors. For 50 ovarian cancers, 25 were epithelial ovarian while 25 were stromal or germ cell tumors. Among 55 cervical cancers, majority were squamous cell carcinomas with only 2 adenocarcinomas. Thirty (17.8%) of FGT cancers had immunohistochemistry performed.

Conclusion: Uterine cancers were commonest followed by ovarian and cervical carcinomas. No decrease in FGT cancer specimens was noted in the COVID pandemic.

Keywords: Cancer care, COVID-19, Gynecology, Oncology, Histopathology.

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## Introduction

The latest national census reports the Pakistan population to be around 220 million. It has been estimated that the annual incidence of cancer is around 170,000 to 200,000 for our population.[1] In order to achieve the goal of improving cancer care, an important step is to establish a national cancer registry. The first cancer registry was initiated in the 1960's by the Armed Forces Institute of Pathology, followed by the National Cancer Registry (NCR) at the Pakistan Medical and Research Council (PMRC) from 1970's to 1990's. This was later reactivated in 2015 under the PHRC. The Punjab Cancer Registry (PCR) was started in 2005 in Lahore, and is currently being managed by Shaukat Khanum Cancer Memorial Hospital. The Karachi Cancer Registry is also active since 2017. [2]

Information retrieved from pathology departments of tertiary care facilities cannot exactly assess the incidence of cancers, yet it assists in determination of the cancer frequency at referral level facilities in the absence of comprehensive national Cancer registry.[3]

In 2018, a comprehensive meta-analysis attempted to deduce recent national trends from published data.[4] A recent report from Pakistan Atomic Energy commission (PAEC) analyses and compares the data from their centers across Pakistan.[5] The PCR and PAEC serve as reliable sources of national data on cancers for

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submission to International Agency for research on cancer (IARC) and World Health Organization (WHO). As per latest PAEC report published in 2019, among the 1278 cancer cases seen among females in the Islamabad center of NORI, the highest frequency was for breast cancers (40.9%) followed by uterus (6.9%), Ovary (6.3%) and cervix (3.2%).[5]

COVID-19 Pandemic emerged in November 2019 in Wuhan, China, and cases started appearing in Pakistan from February 2020. Initially, it was reported among pilgrims from Iran and then other religious congregations seemed to multiply it. A recent publication indicates that a low level of community spread possibly started in early March 2020.[6] With increasing COVID positivity in recurrent waves since then, cancer care has variously been sidelined across the globe. In our hospital, with increasing admissions of seriously sick COVID-19 patients, the number of indoor beds have been reduced for other illnesses. The general outpatient area has been converted to makeshift vaccination center. The Obstetric OPD continued, especially for high-risk women, continued while gynecology OPD and elective gynecological case surgeries were restricted apart from referred, emergent and cancer cases. These improvisations to handle this national emergency due to unexpected viral pandemic resulted in an urgent need to evaluate the effect of the pandemic on cancer diagnosis and treatment. Women, by virtue of their limited access to health care as well as societal limitations, are a particularly vulnerable group. With the onset of COVID-19 Pandemic in Pakistan since March 2020, healthcare facilities are overburdened with COVID cases and care of patients with other illnesses in such facilities possibly compromised.

This study is therefore being undertaken among women presenting with cancers of the female genital tract (FGT) before and after the start of the pandemic to evaluate the effects of repeated lockdown in the care of this particularly vulnerable group and to assess the patient load of gynecological cancers since COVID pandemic in tertiary care facility providing COVID care in the capital.

## Methodology

A retrospective cross-sectional study was conducted after institutional ethics committee approval at the OBGYN department, MCH Center and Pathology department of PIMS, Islamabad, from January 2012 to July 2021. The information was obtained from computer records at PIMS, the histopathology department. All histopathology reports of gynecological cancers during the study period were included. Exclusion criteria were incomplete or incorrect data in computer records. SPSS version 23.0 was used to enter and analyse data.A comparison of rates of different cancers was undertaken for all cases of gynecologic cancers including vulvar, cervical, uterine, fallopian tube, and ovarian whose specimens were submitted to the histopathology lab of PIMS during the study duration. The histopathology of these cancers, stage, age of the patient, and immunohistochemistry was analyzed. The frequency of cancers compared COVID and pre-COVID period. To determine significance, student t-test and chi-square tests have been applied and a p value of $< 0.05$ considered significant.

## Results

The total number of patients found to have genital tract cancers on pathologic diagnosis were 168 over a period of 9 years and 7 months. The cancer specimens seen annually (2012 to 2021) show the temporal trends of genital cancers in the pathology lab in PIMS are shown in table I. Out of 168 specimens, a higher number of cancer specimens (ovary, uterus, cervix, and endometrium) was seen in 2013 (20), 2016 (20), and 2020 (22).

The mean age of patients was 55.45 years, with a range between 8 and 93 years and SD of +14.97 years. Of the 168 genital tract cancers, uterine cancers were 59 (35.1%), cervical were 55 (32.7%), ovarian 50 (29.8%) and 4(2.4%) were miscellaneous varieties. Among the 59 uterine cancers, 53 (32.1%) were endometrial carcinomas, while 6 (4.2%) were stromal tumors. For ovarian cancers, 25 (15.5%) were epithelial ovarian and 25 (15.5%) were stromal tumors. For cervical cancer, the majority were squamous cell carcinomas, 53 (31.5%) and only 2 (1.2%) were adenocarcinomas (Table II).

Thirty (17.8%) specimens of FGT had additional immunohistochemistry (IHC) performed. Among the 50 ovarian cancers, 18 (36%) had IHC, 5 (8.4%) of uterine cancers and 7 (12%) of cervical cancer specimen had IHC.

## Discussion

The female genital tract cancers seen at the pathology lab at PIMS during the previous decade comprised of uterine corpus, cervical and ovarian at almost 30% of total for each category. The data from SKMCH&RC registry reports ovarian cancer at 5% as commonest FGT followed by cervical 4% and corpus uteri 3.6%

rating as 2nd, 4th and 6th most common cancers among females with breast cancer the commonest at 45.1%.[8]

AKU publication in 2016 reported that among 5153 malignant neoplasms in females, ovarian cancer ranked as 4th most frequent followed by corpus uteri at 6th and cervix uteri at 7th most common cancers.

**Table I: Temporal Trends of Genital Cancers at Histopathology Lab.**

| Year | Specimen | | | | | Total |
|---|---|---|---|---|---|---|
| | **Ovary** | **Uterus** | **Cervix** | **Endometrium** | **Miscellaneous** | |
| 2012 | 6 | 4 | 5 | 2 | 0 | 17 |
| | 12.0% | 10.5% | 9.1% | 9.5% | 0.0% | 10.1% |
| 2013 | 11 | 2 | 6 | 1 | 0 | 20 |
| | 22.0% | 5.3% | 10.9% | 4.8% | 0.0% | 11.9% |
| 2014 | 4 | 4 | 4 | 4 | 0 | 16 |
| | 8.0% | 10.5% | 7.3% | 19.0% | 0.0% | 9.5% |
| 2015 | 3 | 1 | 9 | 3 | 1 | 17 |
| | 6.0% | 2.6% | 16.4% | 14.3% | 25.0% | 10.1% |
| 2016 | 6 | 2 | 10 | 2 | 0 | 20 |
| | 12.0% | 5.3% | 18.2% | 9.5% | 0.0% | 11.9% |
| 2017 | 6 | 6 | 5 | 1 | 1 | 19 |
| | 12.0% | 15.8% | 9.1% | 4.8% | 25.0% | 11.3% |
| 2018 | 4 | 3 | 4 | 2 | 0 | 13 |
| | 8.0% | 7.9% | 7.3% | 9.5% | 0.0% | 7.7% |
| 2019 | 3 | 4 | 4 | 1 | 1 | 13 |
| | 6.0% | 10.5% | 7.3% | 4.8% | 25.0% | 7.7% |
| 2020 | 4 | 10 | 5 | 2 | 1 | 22 |
| | 8.0% | 26.3% | 9.1% | 9.5% | 25.0% | 13.1% |
| 2021 | 3 | 2 | 3 | 3 | 0 | 11 |
| | 6.0% | 5.3% | 5.5% | 14.3% | 0.0% | 6.5% |
| Total | 50 | 38 | 55 | 21 | 4 | 168 |

**Table II: Frequency and types of Female Genital tract Cancers.**

| Female Genital Tract Cancers | | N | % |
|---|---|---|---|
| Specimen | Ovary | 50 | 29.8 |
| | Uterus | 59 | 35.1 |
| | Cervix | 55 | 32.7 |
| | Miscellaneous | 4 | 2.4 |
| Ovary | Epithelial | 25 | 15.5 |
| | Stromal | 25 | 15.5 |
| Uterus | Endometrioid | 53 | 32.1 |
| | Serous | 6 | 4.2 |
| Cervix | Squamous Carcinoma | 53 | 31.5 |
| | Papillary serous carcinoma | 2 | 1.2 |

The malignant tumors of the female genital tract are traditionally diagnosed by morphological analysis, using the classical, time tested hematoxylin and eosin stain. To resolve diagnostic dilemmas, especially in respect to therapeutic implications over the past 3-4 decades, various immunohistochemical (IHC) markers are increasingly used in gynecologic onco-pathology and morphology guides toward ordering an optimal panel of IHC markers.[9] Overall 18% of FGT had additional IHC in our study. The highest numbers of IHC's were for ovarian tumors as one third had IHC. IHC is a useful adjunct tool for the subclassification of ovarian carcinomas.[10] This is needed for differentiating primary ovarian from metastatic adenocarcinoma, especially colorectal for deciding upon a specific chemotherapy regimen. Similarly, ovarian sex cord-stromal tumor expresses markers, such as inhibin and calretinin that are negative in carcinomas. It is essential to differentiate a malignant germ cell tumors (GCT) from ovarian carcinoma, in view of different chemotherapy regimens for either tumor as GCT's are relatively highly chemo-sensitive.[10] In selected cases of uterine cancers, IHC is required (to differentiate uterine serous carcinomas from endometrioid adenocarcinomas which was 8% in our study. Additionally, to determine endometrial versus endocervical origin in endometrial carcinomas, IHC is required.

During the COVID pandemic, routine gynecological surgeries almost ceased, especially during the unprecedented lockdown implemented to reduce community transmission.[11] Two recent publications from China report that women with cancers of FGT are especially susceptible to COVID-19 infection with risk of rapid deterioration with even greater need of protection

measures like isolation, masks[12,13] and more recently vaccination. COVID-19 and Cancer Outcome study in the USA in 2020 reports significant reduction in person consultation with greater recourse to telehealth. [14]

Due to dearth of resources compared to the routine heavy workload in our hospital across specialties, telehealth was mainly available for COVID related conditions. Ramirez et al. noted significant modifications of surgical treatments and some degree of surgical delay during the first wave of COVID among women receiving treatment in government verses private facility with similar workloads in the selected facilities being studied in the USA.[15] In our hospital gynecologic cancer services and care pathways were significantly reconfigured with transformed working practices. During OPD limitation of gynecology patients, cancer patients received priority and FGT cancer surgeries continued

Uninterrupted along with obstetric surgeries. This reflects in the similar statistics of FGT in our pathology laboratory as before the Pandemic. Clinical care guidelines for FGT were modified by the international gynecological cancer community with reduction in person visits and prioritizing cancer treatments through online Multidisciplinary tumor board meetings (MDM). [16] At PIMS, the MDM's continued uninterrupted with recourse to Google meet format.

FGT cancer patients were given services on priority in ER as referral patients from clinical and Radio-oncology departments. Cancer surgeries and oncology services continued as per pre-pandemic rate as evident from our results.

The current study did not reveal any reduction in the workload of the pathology department during the pandemic. With the waning of fourth wave in Pakistan, the hesitancy on the part of patients', their relatives and care providers are largely overcome with continued priority care for this vulnerable category of patients. The concern that their treatment may have been delayed or denied does not hold true and is a source of satisfaction for the gynecology and pathology teams undertaking this research.

## Conclusion

During the COVID pandemic the number of female genital tract cancers reported in the pathology department did not reduce in number compared with previous years leading to the inference that the women with female genital tract cancer continued to receive clinical, surgical and diagnostic services despite the limitation of elective gynecological surgeries and outpatient services. Future research to evaluate the clinical impact of COVID on patient perception of the quality of care and their long-term outcomes needs consideration.

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