

THE HISTOPATHOLOGICAL SPECTRUM OF MALIGNANT NEOPLASMS AT A TERTIARY CARE CENTER IN KHYBER PAKHTUNKHWA, PAKISTAN: A FOUR-YEAR HOSPITAL-BASED TUMOR-REGISTRY ANALYSIS

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ABSTRACT

Objective: Population-representative cancer data remain scarce for Khyber Pakhtunkhwa, Pakistan's northwestern province, which receives cross-border referrals from Afghanistan. We analyzed four years of confirmed malignancies at a tertiary-care center to characterize the spectrum of malignancies presenting to the center by site, age, sex, and geography.

Materials & Methods: We retrospectively analyzed consecutive malignant cases entered into the institutional tumor register from 2021 to 2024, each with a histopathological diagnosis, coded tumor topography, and, when recorded, age, sex, and district of residence. Because a hospital register lacks a population denominator, we limited the analysis to case-series comparisons using chi-square, Fisher exact, Mann-Whitney U, and Kruskal-Wallis tests.

Results: Among 1,062 confirmed malignancies, the mean age was 50.8 years (standard deviation 19.1), and 52.4 percent were female ($p=0.118$); men were older (median 55.5 versus 51 years, $p<0.001$). The ten most frequent sites accounted for 70.3 percent of cases, led by central nervous system tumors (14.2 percent), pleural and other intrathoracic sites (8.5 percent), breast (7.8 percent), urinary bladder (7.6 percent), skin (7.2 percent), esophagus (7.0 percent), and colon-rectum (6.1 percent). Site distribution differed by sex ($p<0.001$), with urinary bladder malignancy more frequent among male than female cases (odds ratio 3.45, 95 percent confidence interval 1.98-6.00; $q<0.001$). Central nervous system tumors made up half of all pediatric cases, compared with 12.2 percent of adult cases (odds ratio 7.18, 95 percent confidence interval 4.11-12.53). Most patients (95.2 percent) resided in the province, with 59.6 percent from Peshawar.

Conclusions. This series shows a cancer spectrum led by central nervous system, breast, urinary-tract, aerodigestive, and skin malignancies, supporting the case for a population-based registry and decentralized diagnostic capacity.

Keywords: Hospital-Based Tumor Registry; Histopathology; Epidemiology; Pakistan; Khyber Pakhtunkhwa; Tumor Topography Classification

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INTRODUCTION

Cancer has become a leading cause of premature death worldwide, with an estimated 20 million new cases and 9.7 million deaths in 2022. The burden is rising fastest in low- and middle-income countries.¹ In much of Pakistan, particularly Khyber Pakhtunkhwa (KP), there is no continuously operating population-based cancer registry

with complete case ascertainment, and national frequency data have only recently begun to be consolidated.^{2,3} As a result, the true incidence, stage distribution, and outcomes of common malignancies in the region are inferred largely from hospital series and regional estimates rather than measured directly, with practical consequences for service planning, screening prioritization, and the deployment of scarce oncology resources.

Hospital-based registries, while unable to generate incidence rates, offer an important, immediately available window into the malignancies presenting to a given center.⁴ A tertiary-care center serving as a referral hub aggregates cases from a wide catchment area and captures a broad cross-section of malignancies, including rarer tumors that smaller facilities would miss.⁵ When diagnoses are anchored to histopathology and coded consistently,

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such data describe the relative frequency of tumor sites, the age and sex of affected patients, and the geographic origin of referrals, information that is directly useful for local planning even without denominators.

KP is a large, predominantly rural province with a young population and limited decentralized diagnostic capacity; its major tertiary center in Peshawar draws patients from across the province and, through long-standing cross-border movement, from neighboring Afghanistan. Population-based incidence work for KP has had to be assembled from multiple contributing centers, underscoring how fragmented local ascertainment remains.⁶

We undertook this study to describe the histopathological spectrum of malignant neoplasms in our institutional tumor register over a four-year period (2021–2024), quantifying the distribution of confirmed malignancies by site, the age and sex profile of affected patients, and the geographic origin of cases, while interpreting these findings in light of the well-known limitations of hospital-based data.

MATERIALS AND METHODS

STUDY DESIGN AND SETTING

This retrospective, descriptive analysis included consecutive malignant cases recorded in the institutional tumor register of a tertiary-care hospital in Peshawar, KP, Pakistan. The center serves as a major referral facility for the province, receiving histopathology specimens from its own clinical services and from referring institutions across the region; the register is maintained as part of routine departmental record-keeping.

CASE DEFINITION AND DATA SOURCE

All entries with a histopathologically confirmed malignant diagnosis registered between January 1, 2021, and December 31, 2024, were eligible. Each case in the register had a medical record identifier, a histopathology accession number, and the anatomical tumor location coded to the International Classification of Diseases for Oncology (ICD-O) topography (C-codes). Where recorded, tumor grade or stage descriptors were captured but were incomplete and are not analyzed here.

DATA CLEANING AND HARMONIZATION

Registry data were exported to a spreadsheet and processed programmatically. Because the registry is populated by multiple data entrants, several fields contained inconsistent free text, embedded header rows, and records with data shifted across columns. We therefore applied an explicit, reproducible cleaning rule: a record was retained only if it contained a four-digit registration year within the study window and a syntactically valid ICD-O topography code (of the form C followed by two digits);

records failing these checks were excluded. Of the 1,624 rows in the exported file, 562 were excluded: 411 were specimens accessioned in 2025 (328) or 2026 (83) and therefore fell outside the study window; 142 were specimens accessioned in 2024 that fell within a later, partially uncoded block of the sheet, where the registration-year field was blank and the topography field contained a month abbreviation or was empty; 4 had a valid registration year but an empty topography field; and 5 were repeated in-sheet header or spacer rows. No record was excluded for any other reason. Because 142 of the 289 specimens accessioned in 2024 were excluded on this basis, capture for 2024 is approximately half complete, and the exclusions are therefore not random with respect to calendar time. Sex was harmonized from mixed abbreviations (M/F/m/f/Male/Female) to a single variable. Anatomical sites were mapped from ICD-O topography codes to standard organ-system groupings to avoid fragmentation caused by inconsistent free-text location labels.⁷ Province and district of residence were standardized (for example, variant spellings of Punjab were merged, and cross-border cases were grouped as Afghanistan).

STATISTICAL ANALYSIS

Continuous variables (age) were summarized as mean, standard deviation, median, and range; categorical variables as counts and percentages. Age was recorded for 1,061 of the 1,062 retained cases, and age-based analyses used that denominator. Because a hospital register has no population denominator, no incidence, rate, or risk estimate can be derived; inferential testing was confined to the internal proportional composition of the case series. Age was compared between two groups using a Mann-Whitney U test (with Welch t-test as a parametric check) and across sites using a Kruskal-Wallis test. Categorical associations were tested using Pearson chi-square with Cramér's V as the effect size, applying the Yates continuity correction to two-by-two tables; site categories in these tests followed the groupings in Table 1, and the smallest expected cell count across them was 10.5. Because breast, gynecological, and male genital cancers are anatomically sex-restricted, the sex analysis excluded topography codes C50, C51 to C58, and C60 to C63 (224 cases), leaving 838 cases at non-sex-specific sites and twelve site categories. Male-to-female odds ratios with Woolf 95% confidence intervals were obtained by Fisher's exact test for each of those twelve categories, each of which contained at least 25 cases, and the twelve p values were corrected by the Benjamini-Hochberg false-discovery-rate procedure; q values are reported alongside raw p values. The comparison of age across sites used the thirteen groupings with at least 30 cases. The sex ratio was compared with parity using an exact binomial test. Temporal trends were not tested, since annual counts reflect registration completeness rather than incidence. Two-sided p (or q) < 0.05 was considered significant. Analyses used

Python 3 (pandas, SciPy, Matplotlib).

ETHICAL CONSIDERATIONS

The study used de-identified, routinely collected registry data. Ethical approval was granted by the Institutional Review and Ethics Board of Lady Reading Hospital, Peshawar. The Board waived the requirement for individual informed consent because the study involved only the retrospective analysis of existing anonymized records and posed no risk to patients. No individually identifying information is reported.

RESULTS

COHORT CHARACTERISTICS

After applying the cleaning rules, 1,062 histopathologically confirmed malignancies were available for analysis. Age was recorded for 1,061 of the 1,062 patients. The mean age was 50.8 years (standard deviation [SD] 19.1), with a median of 53 years and a range of 2 to 98 years. Just over half of patients were female (557; 52.4%), and 505 were male (47.6%), yielding a male-to-female ratio of 0.91 (Figure 1). The largest age group was 60-74 years; patients aged 45 years or older accounted for the majority of the series, and pediatric cases (aged 14 years or younger) comprised 5.3% of the total.

DISTRIBUTION BY ANATOMICAL SITE

The relative frequency of malignancies by organ-system grouping is shown in Table 1 and Figure 2. The ten most common sites together accounted for 70.3% of all cases, and the three leading groups accounted for 30.5%. Tumors of the brain and central nervous system (CNS) formed the single largest category (151 cases; 14.2%). The next largest group comprised the pleura and other intrathoracic sites (90 cases; 8.5%), of which 51 (56.7%) had a free-text diagnosis of secondary pleural deposit or mesothelioma, and only two arose in the thymus. Breast cancer (83; 7.8%), urinary bladder cancer (81; 7.6%), skin cancer (76; 7.2%), esophageal cancer (74; 7.0%), and colorectal cancer (65; 6.1%) followed. The relatively high representation of esophageal malignancy is consistent with previous reports of a substantial esophageal cancer burden in this region, where squamous cell carcinoma predominates.^{8, 9} A further 48 cases (4.5%) were of ill-defined or unknown primary origin, reflecting the reality of referral pathology in this setting.

SITE DISTRIBUTION BY SEX

Site patterns differed by sex (Table 2). Among women, breast cancer was the most frequent malignancy (80 cases; 14.4%), followed by CNS tumors (13.3%) and pleural and other intrathoracic lesions (8.3%). Corpus uteri cancer accounted for an additional 42 cases (7.5%), and

cervical cancer for 21 (3.8%). Among men, CNS tumors were most common (77 cases; 15.2%), followed by urinary bladder (12.7%), pleural and other intrathoracic lesions (8.7%), and colorectal cancer (8.3%).

Most patients (1,011; 95.2%) resided in Khyber Pakhtunkhwa. Peshawar district accounted for the most cases (633; 59.6%), consistent with the center's role as the provincial referral hospital. The next largest contributions came from the neighboring districts of Charsadda (58 cases), Nowshera (31), Mardan (30), and Swabi (18), as well as the merged tribal districts of Mohmand (17), Bajaur (16), and Kurram (13). Twenty-nine patients (2.7%) were referred from Afghanistan, and a small minority were from Punjab or had an unrecorded province of residence. The concentration of registered cases from Peshawar indicates substantial reliance on this center for definitive cancer diagnosis among patients in its referral network, and the spread of the remaining cases indicates that many traveled considerable distances.

Comparisons of case-series composition are summarized in Table 3. The overall sex distribution did not differ significantly from parity (52.4% female; exact binomial $p = 0.118$; 95% confidence interval [CI] 0.494-0.555). However, men were significantly older at diagnosis than women (median 55.5 versus 51 years; mean 52.6 versus 49.1; Mann-Whitney $p < 0.001$).

Restricting analysis to the 838 cases at non-sex-specific sites, the distribution of tumor sites differed significantly between men and women ($\chi^2 = 42.1$, $df = 11$, $p < 0.001$), although the effect size was modest (Cramér's $V = 0.224$). Urinary bladder malignancy showed the strongest statistically significant male predominance, and was the only site to remain significant after correction for multiple testing (odds ratio [OR] 3.45, 95% CI 1.98-6.00; $p < 0.001$, $q < 0.001$). Esophageal cancer showed a female excess of borderline significance that did not survive correction (OR 0.53, 95% CI 0.33-0.87; $p = 0.014$, $q = 0.084$), and no other site reached significance once the false-discovery rate was controlled. Age at diagnosis varied markedly across tumor sites (Kruskal-Wallis $H = 186.8$, $df = 12$, $p < 0.001$). CNS tumors affected the youngest patients (median 40 years), followed by breast cancer (median 45 years), while prostate (median 73 years) and urinary bladder cancer (median 69 years) affected the oldest. Consistent with this gradient, CNS tumors were strongly overrepresented among pediatric patients: half of all cancers in children aged 14 years or younger were CNS tumors, compared with 12.2% in adults (OR 7.18, 95% CI 4.11-12.53; $p < 0.001$). Geographic comparisons were largely unremarkable. Patients referred from outside Peshawar were marginally older (median 55 versus 52 years; $p = 0.036$), but site distribution did not differ by geographic origin ($\chi^2 = 21.0$, $df = 15$, $p = 0.136$), nor did pediatric share (5.8% versus 4.4%; $p = 0.382$).

Table No 1: Distribution of histopathologically confirmed malignancies by anatomical site, 2021-2024

Anatomical site (ICD-O grouping)	Cases (n)	Percent
Brain & central nervous system	151	14.2
Pleura and other intrathoracic sites	90	8.5
Breast	83	7.8
Urinary bladder	81	7.6
Skin	76	7.2
Oesophagus	74	7.0
Colon & rectum	65	6.1
Ill-defined / unknown primary	48	4.5
Corpus uteri	42	4.0
Stomach	37	3.5
Prostate	37	3.5
Connective & soft tissue	35	3.3
Kidney & renal pelvis	31	2.9
Trachea, bronchus & lung	27	2.5
Ovary	26	2.4
All other sites combined	159	15.0
Total	1,062	100.0

Groupings are defined by ICD-O topography code: brain and central nervous system (C70-C72); pleura and other intrathoracic sites (C37-C38); breast (C50); urinary bladder (C67); skin (C43-C44); esophagus (C15); colon and rectum (C18-C21); ill-defined or unknown primary (C76 and C80); corpus uteri (C54-C55); stomach (C16); prostate (C61); connective and soft tissue (C47-C49); kidney and renal pelvis (C64-C66); trachea, bronchus, and lung (C33-C34); ovary (C56). The pleura and other intrathoracic grouping is defined by topography alone and therefore includes secondary pleural deposits and mesothelioma (51 of its 90 cases) as well as primary thoracic tumors.

Table No 2: Six most frequent malignancy groups in women and men

Rank	Female (n = 557)	%	Male (n = 505)	%
1	Breast	14.4	Brain & CNS	15.2
2	Brain & CNS	13.3	Urinary bladder	12.7
3	Pleura and other intrathoracic	8.3	Pleura and other intrathoracic	8.7
4	Oesophagus	7.9	Colon & rectum	8.3
5	Corpus uteri	7.5	Skin	7.7
6	Skin	6.6	Prostate	7.3

Table No 3: Comparative analyses of case-series composition. OR = odds ratio; V = Cramér's V; q = Benjamini-Hochberg false-discovery-rate-corrected p-value.

Comparison	Test	Result	p (q)
Sex ratio vs parity	Exact binomial	52.4% female (95% CI 49.4-55.5)	0.118
Age: men vs women	Mann-Whitney U	Median 55.5 vs 51 years	<0.001
Site distribution by sex*	Chi-square	$\chi^2 = 42.1$, df = 11; V = 0.224	<0.001
Urinary bladder: male excess*	Fisher exact	OR 3.45 (1.98-6.00)	<0.001 (<0.001)
Oesophagus: female excess*	Fisher exact	OR 0.53 (0.33-0.87)	0.014 (0.084)
Age across 13 major sites	Kruskal-Wallis	H = 186.8, df = 12	<0.001
CNS tumours: children vs adults	Fisher exact	OR 7.18 (4.11-12.53)	<0.001
Age: outside vs within Peshawar	Mann-Whitney U	Median 55 vs 52 years	0.036
Site distribution by geography	Chi-square	$\chi^2 = 21.0$, df = 15	0.136

*Restricted to the 838 cases at non-sex-specific sites (breast, gynecological and male genital cancers excluded). Because no population denominator exists, all comparisons describe the composition of the registered case series and are not estimates of incidence or risk.

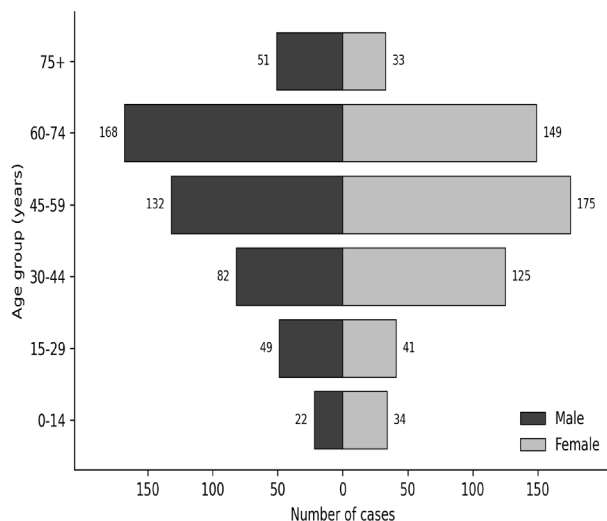


Fig 1: Age and sex distribution of registered malignancies (n = 1,061; age was not recorded for one patient). The 45-59 and 60-74 bands together account for 624 cases (58.8%). Pediatric cases (aged 14 years or younger) number 56 and account for 5.3% of the series. Dark bars, male; light bars, female.

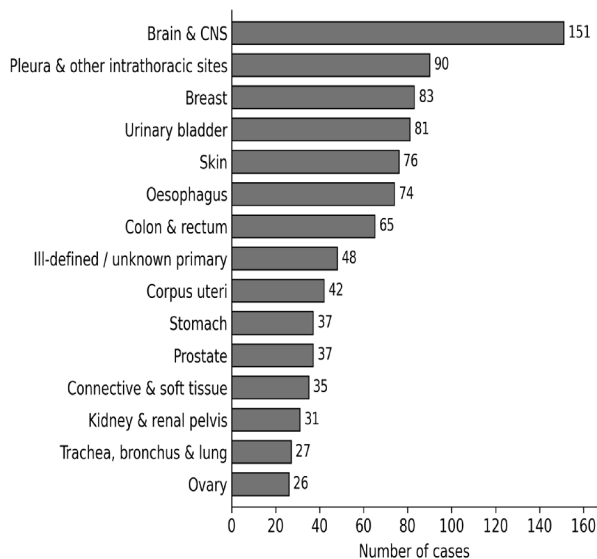


Fig 2: The fifteen most frequent malignancy sites in the four-year series.

DISCUSSION

This four-year analysis of an institutional tumor register identified 1,062 histopathologically confirmed malignancies at a tertiary center in northwest Pakistan. Three features stand out: the prominence of CNS tumors as the largest diagnostic group; the leading position of breast cancer among women and the prominence of urinary-tract and aerodigestive cancers among men; and the heavy geographic concentration of cases in and around Peshawar, with 29 cases (2.7%) referred from Afghanistan.

The finding that CNS tumors constituted the largest group reflects referral patterns rather than an unusual-

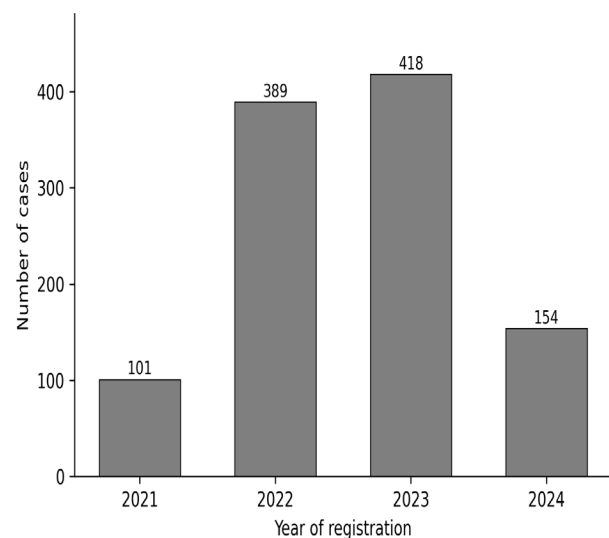


Fig 3: Annual number of registered malignancies. Counts reflect registry establishment and completeness and should not be interpreted as temporal trends in cancer incidence. The low 2021 figure reflects the establishment of the register; the low 2024 figure reflects 142 specimens accessioned in 2024 that had not been coded at the time of extraction and were therefore excluded.

ly high incidence: a tertiary center with neurosurgical and neuropathological capacity preferentially accumulates CNS cases that smaller facilities cannot diagnose or resect. CNS tumors accounted for 28 of the 56 pediatric cases. This sevenfold overrepresentation relative to adults is consistent with CNS tumors being the most common solid tumor of childhood, but it cannot be read as a description of childhood cancer overall: no leukemia was registered in the study window, so the pediatric case mix here reflects which children reach this center. This finding describes the distribution of pediatric malignancies reaching this tertiary center and should not be interpreted as the population-level distribution of childhood cancers in KP. The same referral logic likely explains the share of soft-tissue and unknown-primary cases.

Breast cancer was the leading malignancy among women in this series, accounting for 14.4% of female cases and 7.8% of the whole series. This share is smaller than the approximately 14% of all Pakistani cancer diagnoses attributed to breast cancer in 2020. Pakistan has one of the highest age-standardized breast-cancer incidence rates in Asia, reinforcing the priority of breast awareness and accessible diagnostic pathways for women, who in this setting often present late.¹⁰⁻¹² Esophageal cancer was prominent in both sexes (44 cases, 7.9% of women; 30 cases, 5.9% of men), whereas gastric cancer was more common in men (26 cases, 5.1%) than in women (11 cases, 2.0%). This pattern is characteristic of populations in this part of the world; a Pakistani study found squamous cell carcinoma of the esophagus to be more likely in KP (the former North-West Frontier Province) than in Punjab (odds ratio 2.7, 95% confidence interval 1.2 to 6.2).⁹ Among men, bladder cancer was the only site with

a statistically robust sex difference in our series (OR 3.45), close to the 3.6:1 male-to-female ratio reported in a Pakistani urological series, in which most men had a smoking history and about half the women a history of smokeless tobacco use. Tobacco exposure is not recorded in our register, so that interpretation rests on the published literature and not on these data.¹³ Oral-cavity cancers, by contrast, were uncommon in this series (19 cases, 1.8% of the total; 8 of them in men), although oral cancer ranks among the leading male malignancies in national registry data. That divergence is more plausibly explained by the referral pathways feeding this center than by a genuinely lower local burden.³

The pleural and other intrathoracic grouping warrants a cautionary note. It was defined in advance by ICD-O topography (C37 and C38) rather than by tumor behavior, so it includes secondary pleural deposits alongside primary thoracic tumors. Based on topography codes alone, it might be mistaken for a large burden of primary thymic or cardiac tumors; however, inspection of the underlying diagnoses shows that 51 of the 90 cases (56.7%) were secondary pleural deposits or mesothelioma, and only two arose in the thymus. This underscores the need to review free-text histology alongside topography codes and to use fully coded morphology to materially improve future analyses.

Our overall case mix is broadly consistent with other KP hospital series. A ten-year study of patients from District Dir attending a Peshawar oncology institute likewise found breast, skin and brain tumors among the most frequent diagnoses, although direct comparison is limited by differences in referral base and grouping.¹⁴

The geographic results speak to access. That six in ten patients came from a single district, with the remainder spread across distant districts and a neighboring country, indicates heavy reliance on this single center among those who reach it. We hold no data from other institutions and so cannot describe how cancer diagnosis is distributed across the province as a whole. For patients in peripheral districts, this means longer travel and higher costs. Stage data were too incomplete to analyze, so we cannot show that this translates into later presentation; the modestly older age of patients referred from outside Peshawar is the only signal these data provide. Strengthening district-level pathology and formalizing the evident cross-border patient flow would benefit both patients and regional data quality.

The principal strength of this study is that every case rests on a histopathological diagnosis coded to ICD-O topography, analyzed with an explicit, reproducible cleaning rule over a reasonable four-year span and a substantial case volume. Its limitations are inherent to hospital-based registries.¹⁵ First, these are hospital data without a defined population denominator; we can describe relative frequencies but cannot estimate incidence or risk. Because site proportions within a fixed case series are interdependent, the odds ratios reported here quantify differences in case-mix composition rather than differences in disease risk. Second, referral and

diagnostic selection shape the case mix, most visibly for CNS tumors, so the observed distribution reflects what presents to this center, not community burden. Third, of twelve site-specific comparisons performed, only bladder cancer survived false-discovery-rate correction, and the borderline oesophageal finding should be regarded as hypothesis-generating rather than established. Fourth, the excluded records are not a random subset: most were specimens from 2025 and 2026 that fell outside the study window, but 142 specimens accessioned in 2024 were lost because that block of the sheet had not been coded, so 2024 is only about half captured and the four-year series is weighted toward 2022 and 2023. Free-text fields also limited morphology and grade granularity. Fifth, year-on-year case counts reflect registration completeness rather than temporal trends, which is why no trend testing was attempted. Finally, stage and outcome data were too incomplete to analyze, precluding any survival description.

Notwithstanding these limitations, the study provides a current, locally grounded picture of which cancers present to a major KP referral center and to whom, useful for service planning, training, and awareness efforts, especially for breast cancer in women and tobacco-related cancers in men. More fundamentally, it makes the case for investment in cancer-data infrastructure: full ICD-O morphology coding, systematic capture of stage and outcome, data-entry validation to prevent the field-shift errors we encountered, and ultimately a population-based registry serving the province.

CONCLUSION

Over four years, this tertiary-center tumor register recorded a cancer spectrum led by CNS, breast, urinary tract, aerodigestive, and skin malignancies, with breast cancer the most common malignancy among women and urinary bladder cancer the most common among men after CNS tumors. Cases were heavily concentrated in Peshawar district but drew from across KP and Afghanistan. As hospital-based data, these findings describe referral patterns rather than incidence, but offer a useful contemporary portrait of cancer presentation in northwest Pakistan and a rationale for strengthening regional diagnostic and cancer-registration infrastructure.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Tasneem S	✓	✓	✗	✗	✓	✗
Khan MN	✓	✗	✓	✓	✓	✗
Tariq S	✓	✓	✗	✗	✗	✓
Shah SS	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of
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