

Comparison of presentation and performance status between cancer patients residing in rural and urban areas of Punjab, Pakistan

Muhammad Mohsin Ali¹, Raja Mobeen Ahmed², Raza Gulzar Ghouri³, Hamza Naeem⁴, Alishba Khan and Muhammad Abbas Khokhar⁵

¹ Department of Stroke Medicine, University Hospital Coventry and Warwickshire NHS Trust, ² Department of Medicine, KRL Hospital, Islamabad, ³ Department of Internal Medicine[,] Pakistan Kidney and Liver Institute and Research Centre Lahore, ⁴ Department of medicine, King Edward Medical University, ⁵Department of Internal Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Center Lahore ⁶Department of Clinical Oncology & Radiotherapy, King Edward Medical University, Lahore

ABSTRACT

Background: Cancer has a diverse presentation in the population which may be affected by factors such as equity of healthcare access, distance from cancer care centers, and affordability of cancer treatment. This study aimed to record disparities among the stage of presentation and performance status in patients presenting to a tertiary care cancer center from rural and urban backgrounds.

Methods: An observational cross-sectional study was carried out at a tertiary care cancer center from September 2019 to August 2020. Two hundred and ninety-five patients from both urban and rural areas were included. Patient characteristics were recorded using an interview-based questionnaire and ECOG performance scale, and were similar in both groups. Data analysis was performed using SPSS 24.0, with qualitative statistics determined as frequency and percentages, and quantitative correlations among variables determined by application of a chi-square test with p-value ≤ 0.05 as significant.

Results: In this study, 150 (50.8%) of the participants were female; 52.9% were from urban areas. A significant proportion of the patients had either stage III (20.3%) or stage IV (60%) disease on presentation. More than 50% of the patients had an ECOG performance status score of either 3 (36.9%) or 4 (20%) on presentation or during admission. No significant associations were present between location as urban or rural and stage of cancer (ρ =0.076, p=0.194), or between location and ECOG score (ρ =-0.033, p=0.573).

Conclusion: Many of the determinants of late cancer presentation are similar among urban and rural areas, and patient education, mass screening programs, and the involvement of primary care physicians in cancer care can play an effective role in subverting this problem.

Keywords: cancer disparity; health service accessibility; cancer care; rural-urban background.

Introduction

In a world affected by viral pandemics, various communicable and non-communicable diseases, and strained health resources, cancer remains a slowly yet surely growing menace, with 19.2 million new cases worldwide reported in 2020 alone.¹There is often a significant disparity in the distribution of healthcare resources between rural and urban areas, with rural areas frequently lacking essential health services.

CORRESPONDENCE AUTHOR Hamza Naeem King Edward Medical University, Lahore Email: <u>m.hamza.naeem1234@gmail.com</u> Phone Number: +923343131213 In Pakistan, 67.5% of the population lives in rural areas, whereas in Punjab, the percentage of rural population is 68.7%.² Therefore, most of Pakistan's population is deprived of healthcare facilities available in metropolitan areas, including screening, diagnostic, and management facilities. This is further complicated by a scarcity of oncology facilities in the country overall; with a ratio of only 0.027 medical oncologists per 100,000 population in Punjab alone, adequate cancer care is a privilege few can access or afford .³ A worse survival rate has been demonstrated for rural patients, particularly in the setting of lung, colorectal, prostate, and cervical cancers.⁴ The disparities among



rural and urban populations have been explained by multiple factors, including delayed diagnoses, stage of presentation, treatment modalities, socioeconomic status, and access to health care.⁵ The disparities may also reflect inequalities in smoking and other cancerrelated risk factors, screening, and treatment.⁴

While many factors have been described as causative for rural-urban disparities, studies have shown that uniform access to cancer care can help resolve the disparity in outcomes between rural and urban populations.⁶The impact of socioeconomic deprivation on cancer-related mortality has been found to be considerably greater than the impact of a rural-urban continuum.⁴ The socioeconomic gradients are also much steeper in rural areas than in urban areas, which could be a cause of higher cancer mortality in rural areas.

Rural cancer care centers are practically non-existent in Pakistan, and the vast majority of patients from these areas are referred, often at a time when their disease has metastasized, to urban cancer care centers, which are grossly deficient in facilities as well.³ The disparities in healthcare infrastructure are often discouraging for patients, which practically forces them to fare a far worse prognosis than they would in the presence of adequate facilities. In a cross-sectional survey conducted across three major hospitals in Punjab, it was revealed that rural patients and patients from poor socioeconomic classes are more likely to present with advanced, often incurable cancers .^{7, 8}

The aim of this study was to record disparities among stage of presentation and performance status in patients presenting to Mayo Hospital Lahore from rural and urban backgrounds. Even though comparing survival rates between the two populations was a key goal, it had to be abandoned. This was because of the large number of patients who were lost to follow-up, and the fact that there was no institutional or provincial database of cancer patients that could be used.

Methods

An observational cross-sectional study was carried out in the Oncology & Radiotherapy department of Mayo Hospital Lahore, a 3000 bedded tertiary care facility serving as the primary referral center for oncology patients from Punjab, from September 2019 to April 2020.295 patients from both urban and rural areas were included and it was calculated by random sampling. Inclusion criteria was patients of both genders, aged 18-70 years with a confirmed diagnosis of malignancy who either presented to the Oncology outpatient or were admitted as in-patients in the Oncology ward during the study period. Only those cases in which contact details or data regarding stage of presentation and current performance status were unavailable were excluded. Ethical approval of the study was obtained from the Institutional Review Board of King Edward Medical University Lahore (IRB number 173/RC/KEMU) dated 11-10-2018.

A short-structured questionnaire was used to collect details of the patients. Patient records were utilized to fill the questionnaire; in cases where the patient was admitted, short interviews were conducted to aid the data collection process after due consent. The questionnaire included a section of demographic details such as age, gender, city or district, occupation, income, and BMI; as well as a section on details regarding the cancer diagnosis (including staging, grading, metastasis, family history and treatment attributes); and the ECOG performance status scale. The ECOG (Eastern Cooperative Oncology Group) guidelines for performance status include the following criteria (table 1):

| Table 1: ECOG Performance | Status | Criteria |
|----------------------------------|--------|----------|
|----------------------------------|--------|----------|

| Grade | ECOG Performance Status | | |
|-------|---|--|--|
| 1 | Fully active, able to carry out all pre-disease | | |
| | performance without restriction | | |
| 2 | Restricted in physically strenuous activity but | | |
| | ambulatory and able to carry out work of a light or | | |
| | sedentary nature e.g. light house work, office work | | |
| 3 | Capable of only limited self-care; confined to bed or | | |
| | chair more than 50% of waking hours | | |
| 4 | Completely disabled; cannot carry out any self-care; | | |
| | totally confined to bed or chair | | |
| 5 | Dead | | |

Data analysis was performed using SPSS 24.0, with qualitative statistics determined as frequency and percentages, and quantitative correlations among variables determined by application of chi-square test with p-value ≤ 0.05 as significant.

Results

A total of 295 patients were included in the study, with 150 (50.8%) of the participants being female. Mean age of the participants was 49.46 \pm 15.26 years. More than half of the participants 156 (52.9%) were from urban areas. Average distance between the site of residence and the tertiary care center was 108.2 kilometers, with the farthest distance being greater than 500 kilometers. The body mass index (BMI) of the participants was 21.51 \pm 4.03 kg/m². Majority 183 (62.2%) of the patients were smokers, with the average number of pack years being 28.53 \pm 9.06 years; almost



97% (286 patients) of the patients had a family history of malignancy as well.

Table 2 highlights the main sites of cancers in our patient population in which the most common site for cancer was gastrointestinal and least common was thyroid. A significant proportion of the patients had either stage III (20.3%) or stage IV (60%) disease on presentation (table 3), with distant metastasis present in 48.5% (143/295) of the patients. In the majority of patients, chemotherapy alone was the mainstay of treatment (42.4%), followed by a multimodal approach using chemotherapy and surgical excision in 14.9% of the patients. More than 50% of the patients had an ECOG performance status score of either 3 (36.9%) or 4 (20%) on presentation or during admission.

No significant associations were present between location as urban or rural and stage of cancer (ρ =0.076, p=0.194), or between location and ECOG score (ρ =-0.033, p=0.573). Moreover, no significant differences were present in regards to stage of cancer (ρ =-0.021, p=0.725) or ECOG score (ρ =0.023, p=0.690) against distance travelled by patients to reach the hospital.

| Tuble 2. Main Sites of culletis | | |
|---------------------------------|------------|--|
| System | N (%) | |
| Gastrointestinal | 77 (26.1%) | |
| Breast | 71 (24.1%) | |
| Skin and Soft tissue | 54 (18.3%) | |
| Genitourinary | 50 (16.9%) | |
| Pulmonary | 24 (8.1%) | |
| Central Nervous System | 10 (3.4%) | |
| Bone | 6 (2.0%) | |
| Thyroid | 3 (1.0%) | |
| Total | 295 (100) | |

 Table 3: Stage of Cancer at presentation

| Stage | N (%) |
|-------|------------|
| Ι | 18 (6.1%) |
| II | 40 (13.6%) |
| III | 60 (20.3%) |
| IV | 177 (60%) |
| Total | 295 |



Figure 1: Patient distribution per district

Subgroup analysis showed that urban residents traveled a distance of 63.6±113.4 km to reach the treating facility, whereas rural residents traveled 158.2±170.7 km to reach the same facility. GI malignancies were the most common in rural population (25.2%), followed by breast (23%) and genitourinary malignancies (20.9%). A majority of rural patients presented at either stage IV (55.4%) or stage III (24.5%), with advanced ECOG scores of 3 (36%) or 4 (23%). The frequency of various malignancies by site was almost similar in urban population, with GI malignancies leading at 26.9%, followed by breast (25%) and skin and soft tissue tumors (20.5%); however, the incidence of stage IV cancer presentation was higher (64.1%), and ECOG scores of 2 (34%) and 3 (37.8%) were more prevalent.

Discussion

The rural-urban cancer divide becomes pronounced in lower income countries, where late stages of presentation associated with a poorer prognosis are already the norm. This inequity exists throughout the spectrum of healthcare, with one population based study showing gross inequity in access to surgical care across rural and urban populations ⁹.

Cancer care is no exception to this. In a study on cancer prevalence in rural vs urban regions, and the role of socioeconomic status on presentation, higher cancer incidence was found among rural residents (57.7%) and among those with poor socioeconomic background (65.9%).⁸ Our study was a single center study, and showed an almost equal ratio of rural and urban patients, which we attribute to the fact that our hospital is a tertiary care center and the main point of referral from all other district and tertiary care public sector hospitals.

The incident burden of different cancers in Punjab according to Globocan ranks breast cancer as the most prevalent, followed by lip/oral cavity and lung cancers .^{10,} In our study, breast (24.1%) and gastrointestinal (26.1%) were the most prevalent cancers; the higher prevalence of GI tumors can be attributed to the inclusion of all esophageal, lip/oral cavity, and colorectal tumors under the same system. Most of our patients presented with stage III or IV cancers; this is consistent with multiple studies showing delayed presentations for breast, ^{12, 13} oral cavity ¹⁴ and other cancers in Pakistan, with the major causes being lower socioeconomic class and social factors.

Our study found that more than 50% of the patients had an ECOG performance status score of either 3



(36.9%) or 4 (20%) on presentation or during admission. Higher ECOG scores have been linked to higher incidence of anxiety and depression among cancer patients. ¹⁵Although we found no significant relationship between rural or urban residence and ECOG scores, nevertheless the higher ECOG scores noted during our study pose an important additional risk factor for poorer cancer prognosis.

Rural communities not only suffer from a lack of or inequity of resources; they also face other problems, such as lower enrollment in clinical trials ¹⁶; and lack of access to effective screening programs. ¹⁷ Rural patients have to travel a long distance to reach cancer care facilities in big cities; although government hospitals provide free of cost hospitalization, the brunt of treatment is often borne by the patients themselves.¹⁸

Interestingly, while urban patients in our study traveled a significantly lesser distance compared to rural patients to reach the tertiary care center, the incidence of late stage (III and IV) cancer was slightly higher in the urban population (80.8%) compared to the rural population (79.9%). This indicates that despite closer access to healthcare facilities, including cancer care centers, delayed presentation does not vary between the urban and rural subgroups. This rural-urban disparity in cancer presentation warrants long term prospective studies to delineate a definite impact of rurality on cancer presentation and mortality. In a study on breast cancer presentation across rural and urban areas, rurality was found to be associated with a statistically increased stage of cancer on presentation, as well as an increase in overall mortality .19 Other studies have also shown an increased rate of late-stage cancer diagnosis in rural and deprived areas; this has been attributed to some degree to limited access to cancer care, lower screening rates, and lack of health insurance. ²⁰

In a population based registry analysis of cancer incidence and trends among rural and urban populations in the US, higher incidence of all-site cancers was observed in the urban population, with breast, prostate, GI and thyroid malignancies leading, in contrast to a higher incidence of tobacco and HPV related malignancies in urban populations. The higher overall incidence rate in urban areas did not vary on the basis of sex, ethnicity, or region. Although the overall trends pointed to a decline in cancer incidence over time, the observation was more significant for urban rather than rural areas .²¹ In a similar study from China, the age-standardized incidence of cancer was higher in the urban population compared to the rural population, especially for colorectal cancer and female breast cancer; however the 5-year observed and relative survivals of cancer patients were also higher in the urban population .²² According to India population-based registries, age-standardized cancer incidence rates in urban NCRP cancer registries in India for the period 1990-96 ranged from 97.8 to 121.9 per 100,000 for men and from 92.2 to 135.7 per 100,000 for women. The Delhi registry recorded the highest incidence for both men and women, whereas the rates from the rural population-based registry in Barshi (in the Western Indian state of Maharashtra) were the lowest, at 46.2 and 57.7 per 100,000 for men and women, respectively .²³

Since a country-wide cancer registry is not available in Pakistan, we recommend that a prospective population based study should be carried out to observe trends in cancer incidence, mortality, and survival across rural and urban populations.

An interesting, although hitherto unexplored theme in this regard is the role of primary care physicians in dispensing cancer treatment in rural areas. Primary care physicians with basic knowledge of oncology, having direct communications with oncology colleagues in urban areas as well as a uniform referral system, ²⁴ can made easy the screening and referral process for rural patients. With basic health units (BHUs) distributed in all major rural areas, and the advent of telemedicine, primary care can provide a well-balanced platform for improving cancer care equity in rural areas.

Our study has some limitations: study design is crosssectional, and did not follow the survival rate among patients from urban and rural areas, a statistic which is widely lacking. Moreover, as a single center study from a tertiary center where patients are mostly referred, our presenting population is biased in favor of more urban patients. A large multicenter study, especially in urban areas surrounded by rural centers, with a longitudinal study design would delineate our objectives more clearly. Nevertheless, to our knowledge our study is the first in Pakistan to compare performance status on the ECOG scale, as well as to link urban/rural residency of the patient to stage of cancer and performance status.

Conclusion

In the cancer care continuum, wide disparities exist between urban and rural centers. With most of specialized oncological care in Pakistan focused in urban areas, rural patients have to travel far and wide to reach cancer hospitals. While this is not statistically



linked to poor performance status or worse stage of cancer, it nevertheless provides an important rationale for improving cancer access in rural areas. It also pinpoints that many of the determinants of late cancer presentation are similar among urban and rural areas, and patient education, mass screening programs, and the involvement of primary care physicians in cancer care can play an effective role in subverting this problem.

Acknowledgements: None

Conflicts of Interest: None declared.

Funding: No funding was received for this project

References

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2021 May;71(3):209-49.
- 2. Statistics PB. Area, population, density and urban/rural proportion.
- 3. Khokhar MA, Ali MM, Liaqat S, Moin A, Sarwar HA, Sarwar MZ. A review of access to cancer facilities in Punjab, Pakistan. Cancer Reports. 2020 Jun;3(3):e1245.
- 4. Singh GK, Williams SD, Siahpush M, Mulhollen A. Socioeconomic, rural-urban, and racial inequalities in US cancer mortality: part I–all cancers and lung cancer and part II–colorectal, prostate, breast, and cervical cancers. Journal of cancer epidemiology. 2011 Oct;2011.
- 5. Flowers CR, Nastoupil LJ. Socioeconomic disparities in lymphoma. Blood, The Journal of the American Society of Hematology. 2014 Jun 5; 123(23):3530-1.
- Unger JM, Moseley A, Symington B, Chavez-MacGregor M, Ramsey SD, Hershman DL. Geographic distribution and survival outcomes for rural patients with cancer treated in clinical trials. JAMA network open. 2018 Aug 3; 1(4):e181235-.
- Mahmood N, Mushtaq S, Jamal Q, Hanif M, Akhlaq H, Awan R. Evaluation of Diagnostic and Prognostic Relevance of Single Nucleotide Polymorphism at let-7 micro RNA-binding site of KRAS3/UTR in Oral Squamous Cell Carcinoma. International Journal of Pathology. 2020 Oct 5:20-5
- Bashir U, Wahid K, Baqar M, Khalid F, Vasandani R, Shabbir H. Prevalence of cancer and its types among Urban-Rural populations, the impact of socioeconomic status on cancer in Punjab. Pak J Cancer Prev Cur Res. 2015;2:1-6
- 9. Zafar SN, Fatmi Z, Iqbal A, Channa R, Haider AH. Disparities in access to surgical care within a lower income country: an alarming inequity. World journal of surgery. 2013 Jul; 37:1470-7.
- 10. Khan NH, Duan SF, Wu DD, Ji XY. Better reporting and awareness campaigns needed for breast cancer in

Pakistani women. Cancer Management and Research. 2021 Mar 2:2125-

- 11. Soomro R, Faridi S, Khurshaidi N, Zahid N, Mamshad I. Age and stage of breast cancer in Pakistan: An experience at a tertiary care center. JPMA. The Journal of the Pakistan Medical Association. 2018 Nov 1; 68(11):1682-5.
- 12. Shamsi U, Khan S, Azam I, Usman S, Maqbool A, Gill T, et al. Patient delay in breast cancer diagnosis in two hospitals in Karachi, Pakistan: preventive and life-saving measures needed. JCO Global Oncology. 2020 Jun; 6:873-83.
- 13. Basharat S, Shaikh BT, Rashid HU, Rashid M. Health seeking behaviour, delayed presentation and its impact among oral cancer patients in Pakistan: a retrospective qualitative study. BMC health services research. 2019 Dec; 19:1-9.
- 14. Chiragh S, Ahmed I, Jameel A. Anxiety and depression in cancer patients-a survey in medical oncology department of a tertiary care hospital. Journal of Postgraduate Medical Institute. 2020 Jul 14; 34(1).
- 15. Polite, B.N., Adams-Campbell, L.L., Brawley, O.W., Bickell, N., Carethers, J.M., Flowers, C.R., et al. Charting the future of cancer health disparities research: a position statement from the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology, and the National Cancer Institute. Cancer Research, 77(17), pp.4548-4555.
- 16. Fariha H, Mustafa MS, Misbah M, Khan MR, Shayan M, Muhammad HS, et al. Barriers to Colorectal Cancer Screening in Pakistan. Cureus. 2017; 9(7).
- Aziz Z, Sana S, Akram M, Saeed A. Socioeconomic status and breast cancer survival in Pakistani women. JPMA. The Journal of the Pakistan Medical Association. 2004 Sep 1; 54(9):448-53.
- Obeng-Gyasi S, Timsina L, Bhattacharyya O, Fisher CS, Haggstrom DA. Breast cancer presentation, surgical management and mortality across the rural–Urban Continuum in the National Cancer Database. Annals of surgical oncology. 2020 Jun; 27:1805-15.
- 19. Singh GK, Miller BA, Hankey BF, Edwards BK. Persistent area socioeconomic disparities in US incidence of cervical cancer, mortality, stage, and survival, 1975–2000. Cancer. 2004 Sep 1;101(5):1051-7.
- Zahnd WE, James AS, Jenkins WD, Izadi SR, Fogleman AJ, Steward DE, et al. Rural-urban differences in cancer incidence and trends in the United States. Cancer Epidemiology, Biomarkers & Prevention. 2018 Nov 1; 27(11):1265 74.
- 21. Li X, Deng Y, Tang W, Sun Q, Chen Y, Yang C, et al. Urban-rural disparity in cancer incidence, mortality, and survivals in Shanghai, China, during 2002 and 2015. Frontiers in oncology. 2018 Dec 3; 8:579.



22. Hebert JR, Ghumare SS, Gupta PC. Stage at diagnosis and relative differences in breast and prostate cancer incidence in India: comparison with the United States. Asian Pacific Journal of Cancer Prevention. 2006 Oct 1; 7(4):547.

| HISTORY | | | |
|-----------------------------------|------------|--|--|
| Date received: | 31-07-2023 | | |
| Date sent for review: | 05-09-2023 | | |
| Date received reviewers comments: | 14-09-2023 | | |
| Date received revised manuscript: | 24-09-2023 | | |
| Date accepted: | 26-09-2023 | | |

KEY FOR CONTRIBUTION OF AUTHORS:

- A. Conception/Study/Designing/Planning
- B. Active Participation in Active Methodology
- C. Interpretation/ Analysis and Discussion

23. Ali MM, Khokhar MA, Ahmed HN. Primary care physicians and cancer care in Pakistan: A short narrative. Journal of Cancer Policy. 2020 Sep 1; 25:100238.

| CONTRIBUTION OF AUTHORS | | |
|-------------------------|--------------|--|
| AUTHOR | CONTRIBUTION | |
| Muhammad Mohsin Ali | A,B,C | |
| Raja Mobeen Ahmed | B,C | |
| Raza Gulzar Ghouri | A,B,C | |
| <u>Hamza Naeem</u> | B,C | |