RESEARCH ARTICLE

Distance travelled for brain tumour surgery: A Low- and Middle-income country perspective

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Abstract

Objective: To examine the effect of distance travelled for brain tumour surgery on patient outcomes in an LMIC.

Methods: Data were collected as part of the Pakistan Brain Tumour Epidemiology Study (PBTES) for brain tumour patients who underwent surgery in 2019. Mapping software was used to calculate the distance travelled by each patient from their primary address to the hospital. This was analysed in correlation with outcomes (change in KPS score, current status) and demographic variables.

Results: Of 2366 patients, the median distance travelled across the country was 104 km (IQR: 9.07 - 304). Only 970 (41%) patients had access to brain tumour surgical care within 50 km of their primary address. A total of 372 (15.7%) patients requiring brain tumour surgery had to travel more than 500 km to reach their primary care hospital. Patients travelling more than 50 km for brain tumour surgery had better pre- and post-surgery Karnofsky performance scores ($p<0.001$) than those travelling less than 50 km. The overall survival for these patients was also better (82.4% vs 75.7%, $p= 0.002$) compared to patients travelling less than 50 km.

Conclusion: The distance to a hospital dictates a patient's access to continuity of care through adjuvant chemoradiotherapy and regular follow-ups. Less than half of brain tumour patients in Pakistan had access to brain tumour surgery care within 50 km of their homes. Overall outcomes were significantly better in patients travelling more than 50km for neurosurgical care - suggesting a distance bias effect.

Keywords: Distance travelled, Health disparities, Neuro-oncology, LMIC, Cancer epidemiology.

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Introduction

Cancer burden of disease is currently burgeoning within low- and middle-income countries (LMICs).[1,2] As oncological care becomes more centralised, access to care becomes a primary concern, particularly for follow-up and continuity of care. As part of the Global Surgery initiative and the Lancet Commission, equitable access to surgical care worldwide requires developing nearby centres for oncological surgical care.[3] In LMICs, surgical access is not evenly distributed. According to recent studies on surgical access density, one surgeon is available for 139,299 people.[4] Living outside of surgical care makes timely diagnosis, treatment, and follow-up difficult on top of the issues faced with poor transport systems and low surgeon-to-population ratios. This is because despite developing neurosurgical centres across key urban districts of countries, continued follow-up for post-surgical radiation and chemotherapy is lacking.

Distance travelled for brain tumour care has recently become a topic of interest in many countries with developed healthcare networks. Brain tumours are rare yet devastating diseases, accounting for some of the highest rates of childhood mortality and adult morbidity and mortality in LMICs; surgical access becomes further complicated in neurosurgical care, where it is estimated that one neurosurgeon is available for 0.7-1.4 million people.[5] Essentially, surgical access zones become even smaller for brain tumours due to the overwhelming burden of disease and lack of patient support infrastructure. One key factor here is the distance travelled for brain tumour care. Brain tumour care is a multidisciplinary effort that can often only be dealt within centres concentrated in urban areas of Pakistan, widening the gap in care as most of Pakistan's population lives outside major cities. In Pakistan, in particular, patients travel from far-flung rural areas to larger centres within cities for surgical access. Besides long waiting periods and delays in diagnosis, patients are often unable to continue receiving the standard of care (concurrent chemoradiotherapy) due to an inability to repeatedly

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travel to and from these large, urban centres.[6] The transport accessibility to healthcare is crucial in optimising health outcomes through improving our current models of care. Evidence for distance travelled for brain tumour surgery, and the particular impact that this has on health outcomes is currently lacking in LMICs.

The Pakistan Brain Tumour Epidemiology Study conducted a retrospective cross-sectional study to determine patient characteristics and treatment patterns for neuro-oncological care. Our findings indicate that patients often travel long distances to receive care, despite having neurosurgical centres close to their residences. This prompted a further analysis and discussion into the reasons for travel to receive brain tumour care and the survival outcome associated with travel.

Methodology

As mentioned an article[7] published in this supplement, the Pakistan Brain Tumour Epidemiology Study (PBTES) retrospectively targeted 32 of the largest, high-volume neurosurgical centres across the country from patients who underwent surgical intervention for a brain tumour in 2019. Individuals were excluded if a specific address and district had not been recorded at admission.

Description of variables: Demographic variables were collected from the identified centres through chart review and available hospital records. Distance travelled to the hospital was calculated in kilometres from the patient's primary address to the exact hospital address, as listed, in a straight line (Euclidean distance). This was done to standardise distances travelled as there is no current method of confirming the shortest distance by road networks due to a paucity of geographic data, and self-reported travel times could not be accurately collected. This variable was further stratified according to the district, province, and whether this came under our predefined cut-off (under 50km or above). Patients travelling from outside the country also had their respective countries of origin recorded. Surgical outcomes were recorded according to the preoperative and postoperative (on discharge) Karnofsky Performance Status (KPS) score assessment.[5]

Statistical analysis: The primary endpoints of this study were to quantify the mean distance travelled for brain tumour patients according to province, sector of the hospital where surgery was performed, gender, histopathology, and socioeconomic status. Secondary endpoints were to see rates of adequate access to care through the predefined cut-off distance and the impact of distance travelled on Karnofsky Performance Score (KPS) and current status, as recorded. Univariate and multivariable linear regression analysis was performed to assess the independent factors correlating with distance travelled for brain tumour surgery. Analysis was performed using IBM SPSS Statistics Version 23 and STATA Version 16. P values less than 0.05 were taken to be statistically significant, with 95% confidence intervals of beta coefficients reported.

Results

Out of 2366 patients with recorded addresses, 2265(95.7%) of brain tumour patients came from Pakistan, 98(4.1%) from Afghanistan, and 3(0.1%) from various other countries (Table-1). The median distance travelled for all patients operated on for a brain tumour in 2019 was 104 km (IQR: 9.07 - 304). Regarding the 50 km

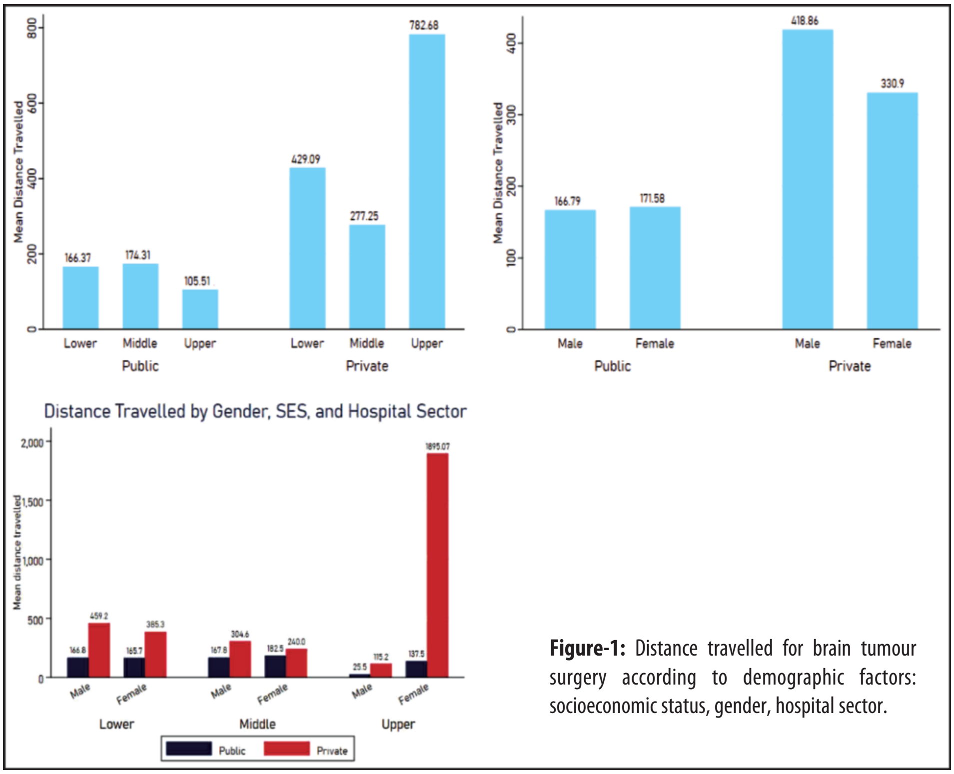

Figure-1: Distance travelled for brain tumour surgery according to demographic factors: socioeconomic status, gender, hospital sector.

Table-1: Mean distances travelled by participants and according to the 50km cut-off.

		Mean Distance Travelled Kilometres	Confidence Intervals		p-value	Distance Cut-off <50 km		>=50 km		p-value
Age Categories	Paediatrics (0-14)	225.49	185.71	265.26	0.021	83	37.40%	139	62.60%	0.031
	AYA (15-39)	263.35	238.07	288.63		337	37.90%	552	62.10%	
	Older Adults (40 & above)	240.38	212.75	268.01		378	43.60%	488	56.40%	
Sector	Public	168.82	156.31	181.32	0.0001	644	40.80%	934	59.20%	0.723
	Private	383.45	347.92	418.97		328	41.60%	460	58.40%	
Gender	Male	252.28	232.66	271.89	0.036	549	39.80%	831	60.20%	0.127
	Female	223.07	199.67	246.47		423	43.00%	561	57.00%	
SES	Lower	217.41	201.69	233.13	0.0001	399	34.80%	749	65.20%	0.0001
	Middle	211.29	188.65	233.92		458	46.10%	536	53.90%	
	Upper	466.67	-170.08	1103.42		7	46.70%	8	53.30%	
Histopathology	Glioma	292.38	261.00	323.76		258	37.70%	426	62.30%	
	Non-neoplastic mass lesions	213.35	144.42	282.27		17	34.70%	32	65.30%	
	Craniopharyngioma	233.31	178.71	287.90		32	34.40%	61	65.60%	
	Medulloblastoma	204.46	153.47	255.45		27	34.60%	51	65.40%	
	Meningioma	184.49	149.11	219.87		142	38.90%	223	61.10%	
	Metastasis	178.22	114.58	241.87		35	47.90%	38	52.10%	
	Pituitary Adenoma	302.88	244.36	361.40		107	46.50%	123	53.50%	
	Vestibular Schwannoma	200.30	148.94	251.66		54	40.90%	78	59.10%	
Glioma	High Grade	287.14	240.14	334.14	0.62	118	39.50%	181	60.50%	0.357
	Low Grade	306.49	259.55	353.43		113	39.50%	173	60.50%	
	Other	239.12	83.78	394.46		2	18.20%	9	81.80%	
Country	Afghanistan	723.55	652.32	794.78		0	0.00%	98	100.00%	
	Others	4436.00	3154.33	5717.67		0	0.00%	3	100.00%	
	Pakistan	213.83	200.46	227.20		972	42.90%	1293	57.10%	
Province	Sindh	139.95	126.14	153.77	0.0001	455	58.00%	329	42.00%	0.0001
	Punjab	175.69	157.50	193.87		421	45.40%	506	54.60%	
	KPK	348.36	299.24	397.48		73	19.90%	293	80.10%	
	Balochistan	418.71	367.98	469.43		23	14.20%	139	85.80%	
	Azad Jammu Kashmir	182.10	103.84	260.36		0	0.00%	12	100.00%	
	Gilgit-Baltistan	1016.57	644.02	1389.12		0	0.00%	14	100.00%	
Status	Alive	268.48	245.14	291.83	0.002	433	38.30%	699	61.70%	0.002
	Deceased	170.87	142.56	199.19		139	48.30%	149	51.70%	

cut-off as an acceptable limit for distance travelled for brain tumour surgery, only 970 (41.08%) patients lived within 50 km of their primary hospital for surgical care. Of even more concern, 372 (15.7%) patients requiring brain tumour surgery had to travel more than 500 km to reach their primary care hospital. We also had patients from other countries, primarily Afghanistan, who travelled to Pakistan for brain tumour surgery (101 (4.2%) of all patients presenting in 2019).

Demographic distribution: Overall, male patients with brain tumours travelled longer distances than female patients for their surgeries (252.28 km vs 223.07 km, p=0.036) (Figure-1). On stratifying the gender of patients according to their documented socioeconomic status (SES), male upper SES patients travelled significantly shorter distances (mean = 89.61, CI: 47.55 - 226.78, p=0.001) for surgical care, with similar distances travelled for men in the lower and middle SES. Conversely, women from the upper SES travelled significantly further for brain tumour surgery (mean = 796.60, CI: 487.38 - 2080.58 , p=0.007) in comparison to lower and middle SES female patients. In the public sector, similar distances were travelled for both men and women for surgery. However, men travelled significantly longer distances to private sector hospitals in comparison to women (418.86 km vs 330.90 km, p=0.007).

As shown in Table-1, the distance travelled for brain tumour surgery was highest in AYA age group compared to paediatric and older adult population patients (p=0.021).

Distance travelled for different brain tumour pathologies: In Figure-2, we can see that the most considerable distance travelled is for low-grade gliomas (306.49 km), and pituitary adenomas (302.88 km). The shortest distances travelled across the country were for metastasis (178.22 km) and meningiomas

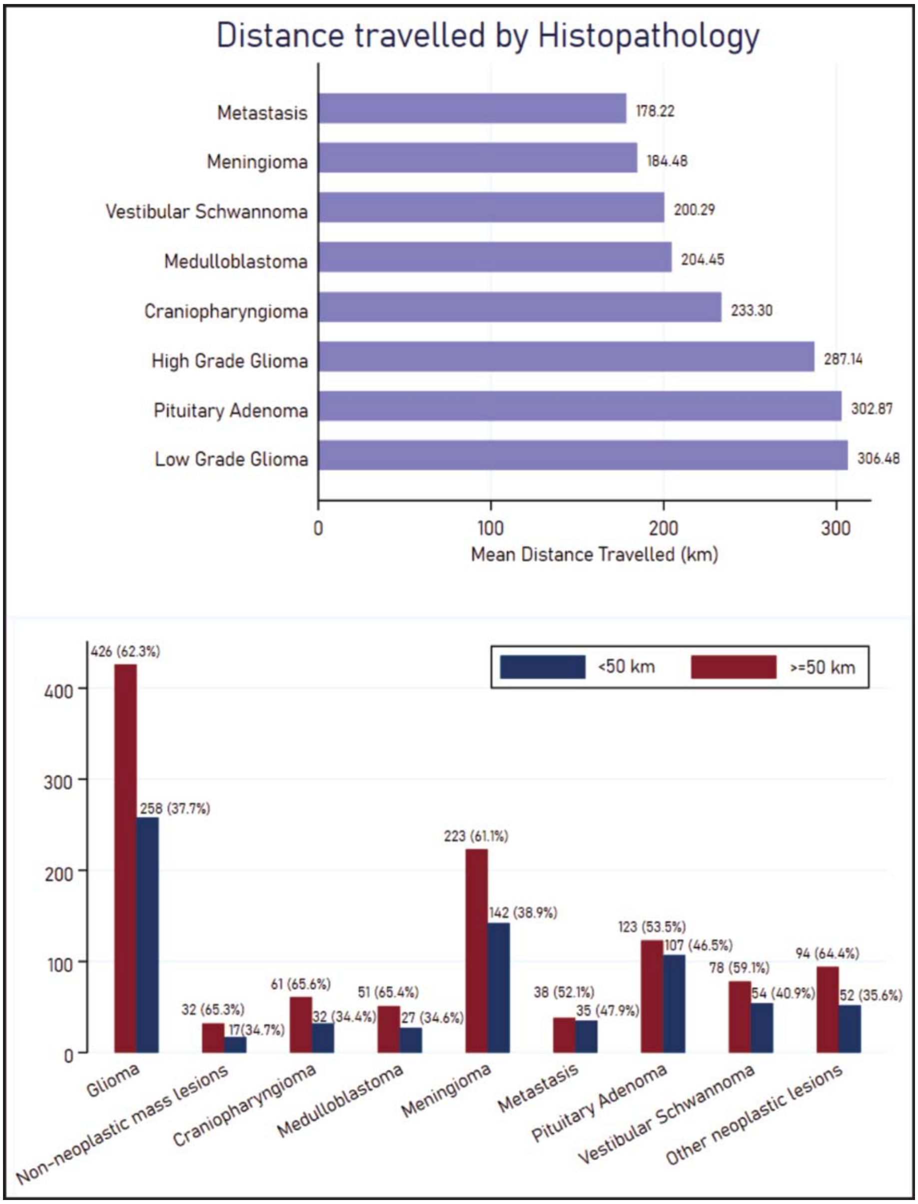

Figure-2: Stratifying mean distance travelled by histopathological diagnosis.

(184.49 km). Between grades of glioma, there was a longer distance travelled for low-grade gliomas compared to high-grade lesions (306.49km vs 287.14km, p = 0.62). Stratifying this according to public and private sector hospitals, we see that for all histopathological subtypes, patients visiting private hospitals travelled further than public sector patients, with the exception of metastatic lesions, where the difference was negligible.

National Overview: Across all provinces, patients from Gilgit-Baltistan (1016.57, CI: 644.02 - 1389.12 km), Balochistan (418.71, CI: 367.98 - 469.43 km), and KPK (348.38, CI: 299.24 - 397.48 km) had a longer mean distance travelled (Figure-3). Although Punjab and Sindh have similar mean distances for surgery, more patients from Sindh travelled within the province for tumour care 782 (99.7%). In contrast, a smaller fraction of patients from Punjab sought care from adjoining provinces, with 834 (90%) of patients remaining within the province. Patients from KPK, 366 (68.6%) and Balochistan, 162 (47.5%) had the lowest rates of within-province care.

Stratifying according to public and private sectors, in most provinces, patients receiving care at private sector hospitals had to travel greater distances for surgical care, except for Sindh, where most of our captured patient population travelled longer distances for care at government hospitals.

Patients visiting private sector hospitals were seen to travel further for brain tumour surgery care compared to public hospital cases (383.45 km vs 168.82 km, p=0.0001).

Surgical Outcomes: In terms of current status, patients who were alive at the time of data collection after brain tumour surgery travelled further than patients who were deceased on the most recent follow-up, regardless of gender (254.59 km vs 150.16 km, p=0.048). On further analysis, patients who were alive and deceased from public hospitals did not significantly differ in the distance travelled (Figure-4). However, patients who were alive at the time of data collection at private sector hospitals travelled significantly further (388.92 km, p=0.001) than patients who were deceased (167.50 km).

According to the 50 km cut-off for adequate access to care, patients who travelled less than 50 km for brain tumour surgery had statistically significantly lower preoperative KPS scores than those travelling further. A similar pattern was seen for postoperative KPS scores.

Linear regression analysis: In our univariate analysis, we identified significant associations of preoperative KPS

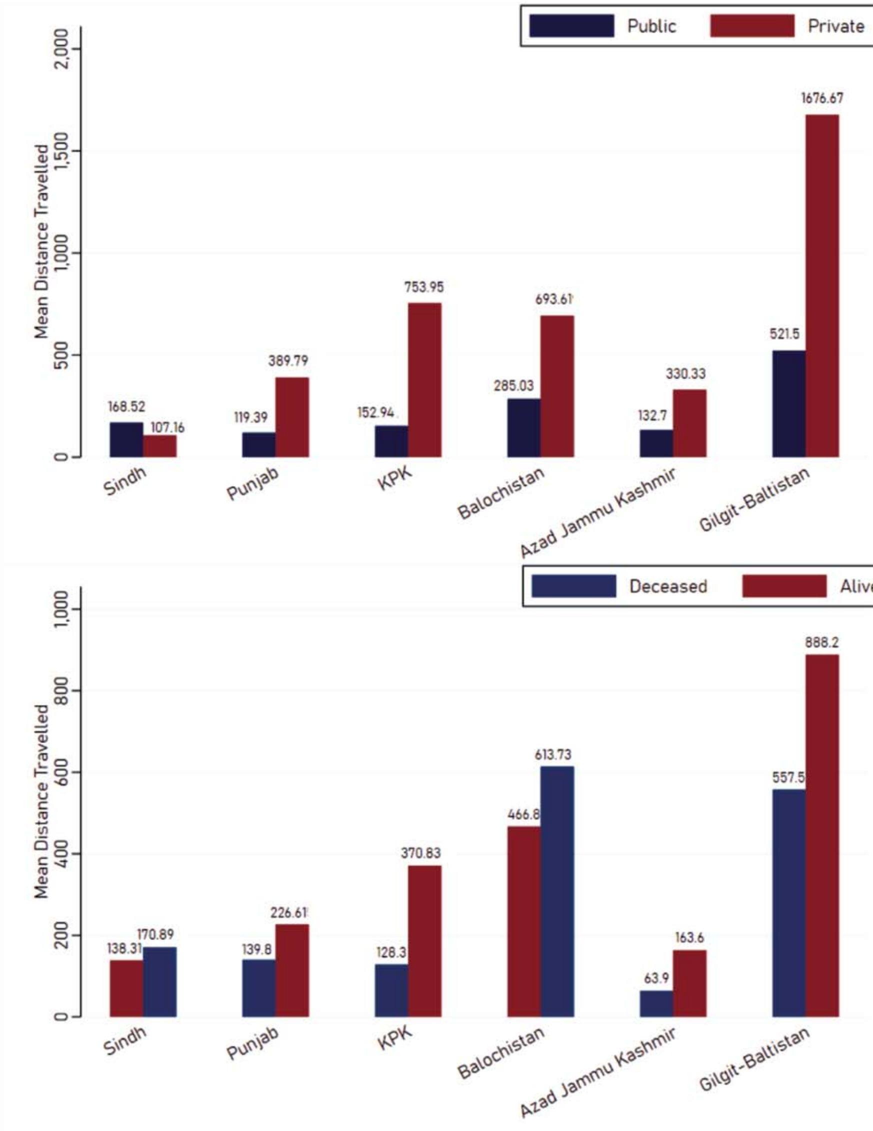

Figure-3: National overview by province and rates for inter- and intra-provincial travel.

	Province travelled to for surgical care			
Patient home province	*Sindh*	*Punjab*	*KPK*	*Balochistan*
Sindh	782 (80%)	2 (0.2%)	0	0
Punjab	70 (7.2%)	852 (90%)	5 (2%)	0
KPK	40 (4.1%)	75 (8%)	251 (96%)	0
Balochistan	79 (8%)	6 (0.6%)	0	77 (100%)
Azad Jammu Kashmir	0	9 (0.9%)	3 (1.1%)	0
Gilgit-Baltistan	6 (0.6%)	6 (0.6%)	2 (0.8%)	0
Total	977	950	261	77

Table-2: Univariate and multivariable linear regression analysis of risk factors for distance travelled for surgical care.

Univariate Model			Multivariable Model	
Characteristics	**Unstandardized Beta coefficient (95% CI)**	**p-value**	**Standardised Beta coefficient (95% CI)**	**p-value**
Age	-.38 (-1.4 - 0.64)	0.467	-2.26 (-3.72 - -0.8)	0.003
Preoperative KPS	3.6 (2.64 - 4.57)	<0.001	0.25 (-1.54 - 2.05)	0.783
Gender				
Male	(reference)		(reference)	
Female	-29.21 (-59.69 - 1.27)	0.06	-16.9382 (-56.82694 - 22.95053)	0.405
Glioma				
High Grade	1 (reference)			
Low Grade	19.35 (-46.59 - 85.28)	0.565		
Histopathology				
Glioma	1 (reference)		1 (reference)	
Non-neoplastic	-79.04 (-186.96 - 28.89)	0.151	43.08786 (-87.12896 - 173.3047)	0.516
Craniopharyngioma	-59.07 (-139.73 - 21.59)	0.151	-25.80835 (-116.2845 - 64.66782)	0.576
Medulloblastoma	-87.92 (-175.14 - 0.7)	0.048	4.229519 (-111.8653 - 120.3243)	0.943
Meningioma	-102.65 (-159.60 - -45.71)	<0.001	-4.415815 (-60.40219 - 51.57056)	0.877
Metastasis	-114.16 (-204.02 - -24.3)	0.013	-35.00104 (-199.8702 - 129.8681)	0.677
Pituitary Adenoma	10.50 (-45.13 - 66.12)	0.711	-11.96197 (-75.11823 - 51.19428)	0.710
Vestibular Schwannoma	-92.09 (-161.47 - -22.7)	0.009	12.11883 (-70.20209 - 94.43975)	0.773
Province				
Sindh	1 (reference)		1 (reference)	
Punjab	35.73 (6.71 - 64.76)	0.016	86.009 (30.60616 - 141.4118)	0.002
KPK	208.40 (170.53 - 246.28)	<0.001	217.5272 (159.173 - 275.8813)	<0.001
Balochistan	278.75 (227.12 - 330.39)	<0.001	328.5047 (251.8534 - 405.156)	<0.001
AJK	42.14 (-131.88 - 216.17)	0.635	42.27514 (-251.264 - 335.8143)	0.777
GB	876.62 (715.3 - 1037.9)	<0.001	673.3935 (376.4192 - 970.3679)	<0.001
Sector				
Public	1 (reference)		1 (reference)	
Private	168.82 (151.12 - 186.52)	<0.001	218.1558 (166.9192 - 269.3923)	<0.001
SES				
Lower	1 (reference)		1 (reference)	
Middle	-6.12 (-34.15 - 21.90)	0.668	-.4299663 (-43.47626 - 42.61633)	0.984
Upper	249.27 (81.16 - 417.37)	0.004	-50.0494 (-278.1993 - 178.1005)	0.667

score, specific histopathology, province, and hospital sector with distance travelled for surgical care (Table-2). However, age, province, and hospital sector remained significant on multivariable linear regression. Higher age predicted for shorter distance travelled (ß = -2.26, p=0.003), whereas patients presenting from Punjab (ß = 86.00, p=0.002), KPK (ß = 217.53, p<0.001), Balochistan (ß = 328.5, p<0.001), and Gilgit-Baltistan (ß = 673.39, p<0.001) were predicted to travel further distance for brain tumour surgery. Similarly, receiving care at a private-sector hospital (ß = 218.16, p<0.001) predicted for further distance travelled.

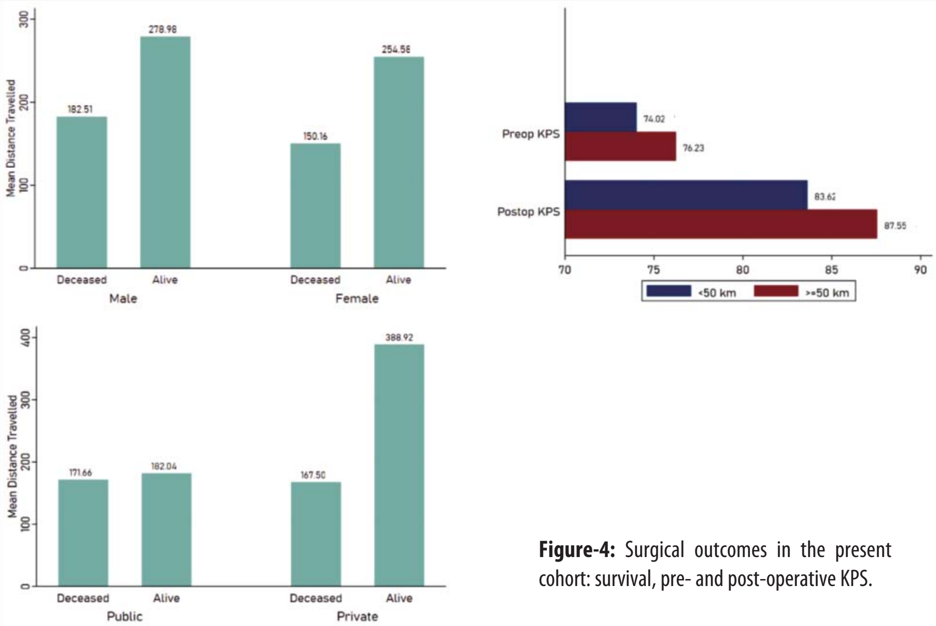

Figure-4: Surgical outcomes in the present cohort: survival, pre- and post-operative KPS.

Discussion

Many studies conducted outside Pakistan have shown that distance of residence from the primary care hospital can affect cancer survival.[3-5] Distance travelled for care is an essential determinant of challenges associated with access to cancer diagnosis and treatment. Various registries, such as the National Cancer Database in the USA, have shown variant patterns of the impact of geographic challenges with worsening cancer stage and survival.[8] Assessing brain tumour care through the lens of the distances travelled by patients to achieve surgical care can help quantify these barriers to access. The effect of distance travelled for oncological care has been widely studied for most other cancers (breast, GI, lung, pancreatic). In a systematic review of the impact of distance travelled for cancer care, three main effects were identified:[9]

Distance-decay association: Patients living closer to their primary cancer hospital had better health outcomes and follow-up rates

Distance-bias association: Patients living further away from cancer care centres showed better survival and follow-up rates

No significant association

The earliest study on glioblastoma care and distance travelled showed that patients living further away from their surgical care hospital were less likely to follow up for chemotherapy required post-surgery.[10] This was further validated as providing the chemotherapy at local care centres improved rates of follow-up. Further studies investigated the precise effect of distance travelled on survival. These suggest a distance-bias association where patients who can travel further and more likely to have better postoperative outcomes and overall survival.[11,12]

It is worth noting that current literature on brain tumour care and the barriers faced by distance travelled comes from countries where centralised cancer registries and health insurance mechanisms are in place; despite existing disparities, the landscape of brain tumour care differs from what is seen in most LMICs. Distance travelled significantly determines whether patients have access to major neurosurgical centres, continuity of care, and adequate follow-ups for catching progressive or recurrent disease on time. To define 'acceptable access to care', we looked through the literature for defined and validated cut-offs for distance travelled for surgical oncology care - while the results were varied, we found it to be appropriate to validate 50 km as an acceptable limit for distance from the primary hospital in cancer patients for optimal follow-up and outcomes, as seen in GI, lung, and breast cancer studies.[13-15]

While most studies in cancer epidemiology have seen a distance-decay association, recent studies for brain tumour surgery have shown a distance-bias effect, effectually taking a different stance from what is usually seen in oncological care. Improved survival for patients travelling longer for surgery may be significantly impacted by the performance status of patients presenting at hospitals, grade of tumour, and disparities in resources and income. These barriers are more pronounced in LMICs, where healthcare systems are still developing and finding their footing. Pakistan, as a case example, has a healthcare industry divided along publicly funded government hospitals providing free surgical care to patients and private-sector hospitals where patients pay out-of-pocket for expensive surgical care. Private insurance companies do exist; however access is limited.

Our data posits a paradoxical image of the impact of distance travelled for brain tumour care, counterintuitive to pre-conceived notions of closer hospital care equalling better survival. However, this effect may be confounded by higher preoperative KPS scores in patients travelling further and having a better baseline status before brain tumour surgery. Patients already suffering from significant morbidity secondary to the tumour may not be able to travel large distances, as needed, to larger centres specialising in neuro-oncological surgeries. Interestingly, the distance travel for surgery was lower for metastatic lesions, whereas the most considerable distances travelled were for low-grade gliomas. This can be explained by the current healthcare system's lack of referrals for patients with metastatic intracranial lesions. Patients often present at later stages of cancer. With advanced morbidity, most of these patients are often not managed at large hospital centres or even referred for a neurosurgical opinion due to current views on the futility of further surgery for the lesion in question. Many patients in such conditions often do not make it to Pakistan's hospitals, opting for at-home care. For primary intracranial tumours, we observed that patients travelled further than the closest site to their residence for neurosurgical care. Socio-cultural norms in Pakistan often result in family and friend referrals to specific hospitals and surgeons; therefore, patients often seek care from surgeons through familial contacts, regardless of travel.

We could also examine the distance travelled between provinces; two points stand out that merit discussion. Public sector hospitals in Sindh had a higher distance travelled than private hospitals. This may be because public sector hospitals in Karachi, the capital of the province and the largest city in the country by population, provide coverage to most of Sindh. Therefore, we can posit that most patients from rural Sindh must travel great distances to reach neurosurgical centres in large cities. Conversely, Punjab had less distance travelled for government hospitals than private-sector hospitals. Secondly, most patients from Balochistan and Sindh that travelled further had poorer survival than patients who travelled shorter distances. This may point to decreased surgical access within these provinces, requiring sick patients with already low preoperative KPS scores to travel further for care.

Our study looked at adequate access to care within resource-limited settings across all brain tumour surgeries. A patient's financial constraints significantly limit access within an LMIC — brain tumour surgery can cost upwards of USD 4,000 at private hospitals in a country where the GDP per capita is USD 1,193.[16] Unfortunately, care at public hospitals, while more affordable, is limited by long-waiting times, limited technological capacity beyond urban centres, and discrepancies in patient follow-ups that can worsen the disease despite adequate surgical treatment. Infrastructural differences between provinces are seen, as patients in Punjab and Sindh showed little out-of-province travel for surgical care, possibly due to well-established and high-volume neurosurgical centres within these areas. However, it is still noteworthy that most patients had to travel upwards of 50 km for brain tumour surgery, possibly due to a lack of nearby and adequate infrastructure.

The current literature supports our findings that patients who travel further for brain tumour surgery are more likely to have better survival and postoperative functional outcomes, as measured by KPS. Recent studies on the effect of travel burden on glioblastoma care in the US have revealed improved overall survival, lower 30-day readmission, and shorter hospital stays in patients travelling longer to higher-volume centres.[11] These, however, may be more impacted by the financial burden of travelling and affording surgical care for brain tumours, as revealed in a recent analysis by Bird et al.[10] CNS tumours in the adolescent and young adult (AYA) age group have also shown to be associated with improved survival when travelling longer distances to facilities more experienced with treating CNS tumours.[17]

Our study is limited by incomplete follow-ups and patient records, due to which time-to-event survival analysis was not possible. We could not evaluate the impact of distance to centres where radiation and chemotherapy were administered; this could help further understand its role in neuro-oncological care in Pakistan. This study could also not account for economic factors beyond SES, such as specific income quartiles. Despite these limitations, this is the most comprehensive current estimation of brain tumour patients receiving surgical treatment across the country. Developing a central registry body would provide a more expansive overview and build upon the present study's findings.

Conclusion

Distance travelled for brain tumour surgery determines whether patients can continue adjuvant treatment and follow-up with physicians. Less than half of brain tumour patients in our report had access to neurosurgical oncology care within 50 km of their primary addresses. Patients travelling farther distances to surgical centres had better outcomes, suggesting a distance bias effect. This is similar to what has recently been reported in other countries regarding the impact of distance travelled on brain tumour care, with better outcomes for patients travelling further distances. This study presents the first analysis and overview of the current access to neuro-oncological surgery for patients in Pakistan.

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Conflict of Interest: None to declare.

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