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Overview

Comparison of Epidemiology and Outcomes in Neuro-Oncology Between the East and the West: Challenges and Opportunities

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Abstract

Although neoplasms of the brain and central nervous system (CNS) are relatively uncommon, comprising only 1–2% of the overall cancer burden, they represent a substantial source of morbidity and mortality worldwide. The age-adjusted annual incidence of CNS tumours is reportedly low; however, there is substantial global variability in its incidence, with nearly a five-fold difference between regions with the highest rates in developed countries in the West and those with the lowest rates in developing countries in South-East Asia, including India, possibly attributable to key differences in environmental factors, genetic susceptibilities and cultural practices, as well as resource constraints in low–middle income countries precluding precise ascertainment and accurate diagnosis. The burden of CNS tumours is further compounded by the fact that they require highly specialised and skilled multidisciplinary care, including access to modern neuroimaging, neurosurgery, neuropathology and molecular biology, radiotherapy, chemotherapy and rehabilitation services, which may not be widely available in an integrated manner in large parts of the world with a large variation in clinical pathways, non-uniformity of care and resultant heterogeneity in clinical outcomes. CNS tumours encompass a heterogeneous spectrum of histopathological entities with differences in presentation, distinct molecular/genetic alterations, diverse biological behaviour and varying clinical outcomes. Survival is highly dependent on histology, grade and molecular biology, but varies widely across continents, even for the same tumour type and grade. In general, survival is higher in children with primary brain tumours than in adults, largely due to the differences in histological distribution across age groups. However, there is widespread variability, with 5-year survival for paediatric brain tumours being <40% in some low–middle income countries compared with 70–80% in the developed world. This review compares the descriptive epidemiology and clinical outcomes of primary brain tumours between the East and the West that pose unique challenges but also provide new opportunities in contemporary neuro-oncological practice.

Key words: Brain tumours; epidemiology; multidisciplinary; neuro-oncology; outcomes

Introduction

Tumours of the brain and central nervous system (CNS), although uncommon, comprising only 1–2% of the overall cancer burden, represent a common source of morbidity and mortality worldwide [1,2]. Substantial variation in brain tumour epidemiology, incidence, histological spectrum and mortality has been reported between countries across the world [1,2]. The age-adjusted annual incidence of CNS tumours is reportedly low (4.63 per 100 000 person-years); however, there is substantial global variability in its incidence, with nearly a five-fold difference between regions with the highest rates, such as developed countries in the West (North America and Western Europe), and those with the lowest rates in developing countries in South-East Asia, including India [1,2]. The reasons behind these differences are not entirely clear. Several factors, such as key differences in environmental factors, genetic susceptibilities, cultural

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practices, demographic structure and the age pyramid, as well as availability and access to resources in different healthcare systems, could result in regional differences in the burden of brain and CNS tumours [1,2]. The burden of CNS tumours is further compounded by the fact that they require highly specialised and skilled multidisciplinary care (Figure 1), including access to modern neuroimaging, neurosurgery, neuropathology and molecular biology, radiotherapy, chemotherapy, rehabilitation and other ancillary services, which may not be widely available in an integrated manner in large parts of the world, with resultant differences in clinical care pathways and outcomes. This review compares the descriptive epidemiology, including the histopathological spectrum, and clinical outcomes of CNS tumours between the East and the West. Differences in sociocultural milieu and resource limitations in low–middle income countries (LMICs) do pose unique challenges, but also provide new opportunities to develop and foster multidisciplinary care in contemporary neuro-oncological practice through mutual co-operation and collaboration between the developed world in the West and developing countries from the East.

Brain Tumour Epidemiology

Data Sources

The major data sources for this article include GLOBOCAN 2018 report [1], Global Burden of Diseases, Injuries, and Risk Factors (GBD) 2016 report [2], Central Brain Tumor Registry of United States (CBTRUS) statistical report 2011–2015 [3], Million Death Study report [4] and CONCORD-3 update [5].

Global Disease Burden

Tumours of the brain and the CNS comprise only 1–2% of the overall cancer incidence, yet globally they contribute a substantial burden of disease. In total, 296 851 new cases (1.6% of overall cancer incidence) and 241 037 deaths (2.5% of overall cancer-related mortality) from brain and CNS tumours were reported globally in 2018 [1]. According to the latest GBD report [2], there were 330 000 (95% uncertainty intervals 299 000–349 000) incident cases of CNS cancer and 227 000 (95% uncertainty intervals 205 000–241 000) deaths globally in 2016. The age-standardised incidence rates (ASR) of CNS cancer increased by 17.3% (95% uncertainty intervals 11.4–26.9) over time between 1990 and 2016 (2016 ASR of 4.63 per 100 000 person-years [95% uncertainty intervals 4.17–4.90] with India, China and the USA accounting for most cases [2]. The annual incidence, mortality and disability-adjusted life-years (DALY) burden with 95% uncertainty intervals from brain and CNS tumours in selected countries (representing the West and the East) are provided in Table 1. The incidence of CNS cancer increases with each quintile of socio-demographic index – a composite indicator of fertility, education and income – with the highest ASR of 6.1 (95% uncertainty intervals 5.7–7.5) per 100 000 person-years in the highest quintile. Apart from high mortality, CNS cancer was responsible for 7.7 million (95% uncertainty intervals 6.9–8.3) DALYs globally in 2016, reflecting high levels of associated morbidity.

Regional Disease Burden

Data from the West (USA, Canada and Western Europe)

As per the latest CBTRUS statistical report [3], brain and other CNS tumours have now replaced blood cancer as the most common neoplasm in the 0–14 years age group in the USA, with an average annual age-adjusted incidence of 5.65 per 100 000 population. In infants and children, the annual age-adjusted mortality for these tumours was 0.72 per 100 000 population (the eighth most common cause of death overall and the leading cause of cancer-associated death). In the subset of patients aged between 15 and 39 years, CNS was the second most common site of cancer in men and the third most common site of cancer in women (ASR of 11.2 per 100 000 population). In this subgroup of adolescents and young adults, the annual age-adjusted mortality was 0.96 per 100 000 population (the 13th most common cause of death overall and the second most common cause of cancer-related death). In the population of patients aged 40 years or more, CNS tumours (both benign and malignant) represented the eighth most common cancer among men and the fifth most common cancer among women (ASR of 44.4 per 100 000 population). In 2016, the annual DALY burden of brain and CNS tumours in the USA was estimated to be 453 457 (95% uncertainty intervals 410 642–491 397) [2]. Tumours of the brain and CNS encompass a heterogeneous spectrum of histopathological entities [6], with differences in presentation, distinct molecular/genetic alterations, diverse biological behaviour and varying clinical outcomes. As per the recent CBTRUS report [3], the histopathological spectrum of CNS tumours varies considerably between adults and children. Overall, the most common histology was meningioma (37.5%) followed by pituitary adenoma (16.5%) and glioblastoma (14.7%). Meningioma constituted the most common benign histology (53.1%), whereas glioblastoma was the most common malignant histology (47.7%). Among children and adolescents (0–19 years), pilocytic astrocytomas (15.3%), tumours of the pituitary (12.2%), malignant gliomas - not otherwise specified (11.4%), embryonal tumours (10.4%), other astrocytomas (7.8%) and neuronal/mixed glioneuronal tumours (7.3%) were the common histological entities. Medulloblastoma was the most common (63.3%) type of embryonal CNS tumour.

The Canadian Cancer Registry recently published data pertaining to CNS tumours among patients registered in Canada from 2009 to 2013 [7]. Glioblastoma constituted the most common histology in the adult population, with an estimated incidence rate of 4.06 per 100 000 population. Among children, embryonal tumours comprised the most common histology, with an estimated incidence rate of 0.74 per 100 000 population. Similar to other countries from the developed world, brain and other CNS tumours are

Fig 1. Recommended multidisciplinary care model of a comprehensive neuro-oncology programme.

responsible for 56 379 (95% uncertainty intervals 45 459–63 690) DALYs every year in Canada, reflecting high morbidity [2]. Unlike North America, there is a lack of brain tumour-specific registries in some of the Western European countries, precluding accurate data capture on the true incidence of primary brain and CNS tumours. In the UK, 5053 (95% uncertainty intervals 3866–5377) new brain tumour cases were estimated to occur in 2016, with 4194 (95% uncertainty intervals 3163–4432) reported deaths, resulting in a 111 667 (95% uncertainty intervals 89 431–117 828) DALY burden [2]. The ASR of glioblastoma was seen to double in the UK from 2.4 to 5 per 100 000

Table 1
Incidence, deaths and disability-adjusted life-year (DALY) burden with 95% uncertainty intervals from tumours of the brain and central nervous system in 2016 in selected countries from the West and the East (all data were extracted from the Global Burden of Disease study [2])

Country	Incidence in 2016 (95% uncertainty intervals)	Deaths in 2016 (95% uncertainty intervals)	DALY burden in 2016 (95% uncertainty intervals)
USA	24 725 (22 447 to 26 908)	16 779 (14 745 to 17 556)	453 457 (410 642 to 491 397)
Canada	3501 (2801–3952)	2104 (1737–2356)	56 379 (45 459 to 63 696)
Germany	8300 (6013–9781)	6104 (4487–6938)	150 993 (117 742 to 172 869)
UK	5053 (3866–5377)	4194 (3163–4432)	111 667 (89 431 to 117 828)
India	23 344 (21 446 to 28 329)	21 042 (18 847 to 25 993)	811 288 (731 493 to 1 008 612)
China	106 207 (96 980 to 119 885)	59 120 (53 264 to 66 813)	193 3243 (1 756 995 to 2 196 524)
Japan	8953 (6838–9761)	2619 (2059–2845)	67 929 (56 427 to 76 950)

population, with absolute numbers rising from 983 cases in 1995–2531 cases in 2015 [8]. Germany reported 8300 (95% uncertainty intervals 6013–9781) new cases of brain and CNS tumours in 2016, with 6104 (95% uncertainty intervals 4487–6938) estimated deaths and a resultant 150 993 (95% uncertainty intervals 117 742–172 869) DALYs [2]. The histological distribution of cases in Germany suggested that glioblastoma was the most predominant histology among adults, whereas embryonal tumours predominated in children. Among children, data collected between 1990 and 1999 [9] showed that the common brain tumours in descending order were astrocytomas (41.7%), medulloblastomas (18.1%), ependymomas (10.4%), supratentorial primitive embryonal tumours (6.7%) and craniopharyngiomas (4.4%).

Data from the East (India, China and Japan)

India and China contribute to the major burden of brain and CNS tumours from the proverbial East and, together with Japan, adequately represent the spectrum of developmental indices usually seen in the East. However, it may be pertinent to note that epidemiological data on brain and CNS tumours from the East are primarily derived through geographically defined population-based cancer registries, with poor and variable coverage across the country and resultant biased estimates.

As per GLOBOCAN estimates [1], the estimated number of incident cases of CNS tumours in India in 2018 was 28 142, with 24 003 reported deaths. According to the GBD report [2], the estimated number of incident cases in India in 2016 was 23 344 (95% uncertainty intervals 21 446–28 329) with 21 042 (95% uncertainty intervals 18 847–25 993) reported deaths. The estimated numbers of DALYs related to brain and CNS tumours in India in 2016 was 811 288 (95% uncertainty intervals 731 493–1 008 612) [2]. The GLOBOCAN estimates 76 494 new cases of brain and CNS tumours with 63 860 deaths from China in 2018 [1]. By contrast, the GBD reported 106 207 (95% uncertainty intervals 96 980–119 885) new incident cases and 59 120 deaths (95% uncertainty intervals 53 264–668 130) with a resultant 1 933 243 (95% uncertainty intervals 1 756 995–2196 524) DALYs related to brain and CNS tumours from China in 2016 [2]. The GBD estimates are very similar to the data from the National Central Cancer Registry of China [10], which reported 101 600 incident cases and 61 000 deaths from CNS tumours in 2015 in China. Unlike India and China, which are still developing countries, Japan represents a developed economy from the East with a high sociodemographic index. As per GLOBOCAN [1], Japan was estimated to have 6319 new incident cases of brain and CNS tumours, with 2817 reported deaths in 2018. The GBD report [2] estimated 8953 (95% uncertainty intervals 6838–9761) new cases and 2619 (95% uncertainty intervals 2059–2845) deaths, with an estimated CNS tumour-related DALY burden of 67 929 (95% uncertainty intervals 56 427–76 950) from Japan in 2016.

The histological spectrum of brain tumours may differ substantially between some countries. Analysis of the records of the Brain Tumor Registry of Japan [11] between 1984 and 2000 showed that glioma and meningioma were less frequent, whereas pituitary adenoma and germ cell tumours were more frequent in Japan, compared with the corresponding CBTRUS data. The most striking difference is for intracranial germ cell tumours [12], which constitute 10–13% of all primary CNS neoplasms in children and adolescents (0–19 years) in Japan compared with only about 3% in the West. The predominance of gliomas in the Western population and that of relatively uncommon tumours such as germ cell tumours in the Far East could be due to hitherto undiscovered genetic susceptibilities, environmental influences and cultural practices. Recent data [13] suggest that nearly 40% of high-grade gliomas in children in Jordan are related to biallelic mismatch repair deficiency due to the high prevalence of consanguinity [14]. Cross-sectional data [15] from China collected between 2005 and 2006 show that primary brain tumours had a prevalence rate of 24.56 per 100 000 population, with a higher prevalence seen in women compared with men (30.57 versus 18.84 per 100 000 population). More than half (52.57% of reported tumours were either gliomas or meningiomas. Among patients aged 0–19 years, gliomas accounted for 55.56% of cases. Between the ages of 20 and 59 years, the case load was comprised primarily of pituitary adenomas (45.12%) and gliomas (31.10%).

India contributes significantly to the global burden of brain and CNS tumours. Data collected from five population-based cancer registries (Mumbai, Chennai, Bengaluru, Delhi and Bhopal) between 1982–1983 and 2002–2003 revealed an increase in the incidence of primary CNS tumours over time, with ASR varying between 2.66 and 3.08 per 100 000 in men and 1.46 and 2.17 per 100 000 in women [16]. The Million Death Study survey [4] estimated that overall 3400 paediatric deaths in India in 2010 were attributable to CNS tumours, with a resultant mortality rate of 9 per 100 000 population with 95% confidence interval ranging from 6 to 12, a rate distinctly higher even than the incidence reported by several cancer registries in India. Explanatory factors include the difficulty in diagnosing CNS tumours without expensive diagnostic imaging and variation between cancer registries in capturing data on benign brain tumours. There exists a paucity of high-quality cross-sectional data documenting the histological spectrum of brain and CNS tumours across various age groups at the national level. Data on the histopathological spectrum are largely restricted to tertiary-care hospital-based registries or pooled multi-institutional collaborative studies, with the potential of significant referral bias. The most robust estimate of the histopathological spectrum in the paediatric population comes from a pooled multi-institutional analysis [17] of 3936 children (<18 years of age) with primary paediatric brain tumours registered during different time intervals at seven different tertiary-care hospitals in India. On average, paediatric CNS tumours accounted for 14.8% (range 10–21%) of all intracranial tumours. Astrocytomas were the most common paediatric brain tumours (34.7%) followed by embryonal CNS tumours (22.4%) and craniopharyngiomas (10.2%). The largest dataset on descriptive epidemiology of brain and

CNS tumours [18] from India was reported from a hospital-based brain tumour registry that recorded 4295 primary intracranial tumours over a 5-year period (2010–2014). Among children, astrocytomas (25.1%), embryonal tumours (20.6%) and ependymomas (14.8%) were the most frequently reported histologies. In adults, meningiomas (23.2%), glioblastomas (15.5%) and nerve sheath tumours (12.7%) were common. Glioblastomas showed a male predilection, whereas meningiomas were more commonly seen in women. The only population-based cancer registry data [19] on the histological spectrum of malignant brain tumours in India come from Delhi, which documented 1989 cases of CNS cancers between 2003 and 2007. Diffuse gliomas, including astrocytomas, oligodendrogliomas and glioblastomas, accounted for the vast majority (>60%) of malignant CNS tumours, followed by medulloblastomas (6.3%) and ependymal tumours (2.2%). Histology-specific differences in regional incidence of malignant CNS tumours have been reported, with astrocytic tumours showing the broadest variation in incidence regionally across the globe [20]. Representative histopathological spectrums of CNS tumours in the overall population and children in the USA and India are depicted in Figure 2.

Survival Outcomes

In the largest survival analysis [5], involving 656 659 adults with tumours of the brain and CNS registered between 2000 and 2014 in 269 cancer registries across 59 countries, the age-standardised 5-year net overall survival was in the range of 20–40%. The trends in 5-year survival between 2000–2004 and 2010–2014 were generally flat, although some countries, including the USA, Canada, Western Europe, India, China and Japan, documented a substantial increase in survival over time. Similar analyses involving 66 814 children with primary brain tumours showed substantial geographic variation. The highest age-standardised 5-year net survival rate for childhood brain tumours was reported from the Nordic countries (>80%), followed closely by the USA, Canada, Western Europe and Japan (70–79%). Survival was slightly lower at 60–69% in lesser developed countries from Asia and Eastern Europe, but was lowest (<40%) in some developing countries (China, Thailand, Mexico). Survival trends between 2000–2004 and 2010–2014 were either stable or increasing in most developing countries, reflecting improvement over time. Age-standardised 5-year net overall survival with 95% confidence intervals in adults and children with tumours of the brain and CNS for selected countries representing the West and the East are compared in Table 2.

Guidance from the West

Despite several challenges unique to the sociocultural milieu of developing countries in the East, compounded by significant resource limitations, the inferior survival of patients with tumours of the brain and CNS compared with the developed world, warrants concerted efforts from all relevant stakeholders to increase awareness regarding CNS tumours for early diagnosis: create patient advocacy and support groups to pressurise governmental organisations to augment budgetary allocation towards necessary healthcare spending and capacity-building; establish comprehensive neuro-oncology programmes at the national and regional level, including the development of clinical care pathways; adopt evidence-based management guidelines with regular audits; and engage in fruitful collaboration with international peers to improve outcomes in contemporary neuro-oncological practice.

Raising Awareness and Creating Patient Advocacy Groups

It is widely acknowledged that common neurological signs and symptoms, such as headache, vomiting, visual disturbance, imbalance and seizures, are not specific to tumours of the brain and CNS, leading to an inordinate delay in referral for imaging and diagnosis. The HeadSmart initiative [21], initially launched in the UK to increase awareness about brain tumours in children and young people, led to a significant reduction in the median time to diagnosis of brain tumours. Since 2012, the HeadSmart campaign has been adopted in the European Union through partnerships between patient advocacy/support groups and healthcare professionals and is also being extended to other developing countries in the East. Patient advocacy groups help patients, their families and their caregivers better navigate the cancer landscape. These groups work to ensure that cancer patients receive appropriate and timely care, education, financial assistance and logistic support. The brain tumour community is a unique, underserved population that has not seen significant improvements in survival over the last four decades. In the search for effective treatments for brain tumours, non-profit patient advocacy organisations can identify and fill the gaps that the for-profit sector and the government have not been able to address. The International Brain Tumour Alliance – a unique global network for brain tumour patient and caregiver groups around the world – works alongside researchers, scientists, clinicians, nurses, allied healthcare professionals and the industry to engage in advocacy, raise awareness and share information. The evolution of such organisations and their impact in neuro-oncology has been systematically reviewed and summarised recently [22]. Brain tumour support groups created through former patients and their families are an immense source of strength and information to the newly diagnosed patients and their caregivers.

Neuro-Oncology Care Pathways

As part of an action plan to improve cancer care throughout the National Health Service in the UK, the National Institute for Health and Care Excellence (NICE) has developed a guidance document [23] describing how healthcare services for people with brain and other CNS tumours should be organised. One of its most important

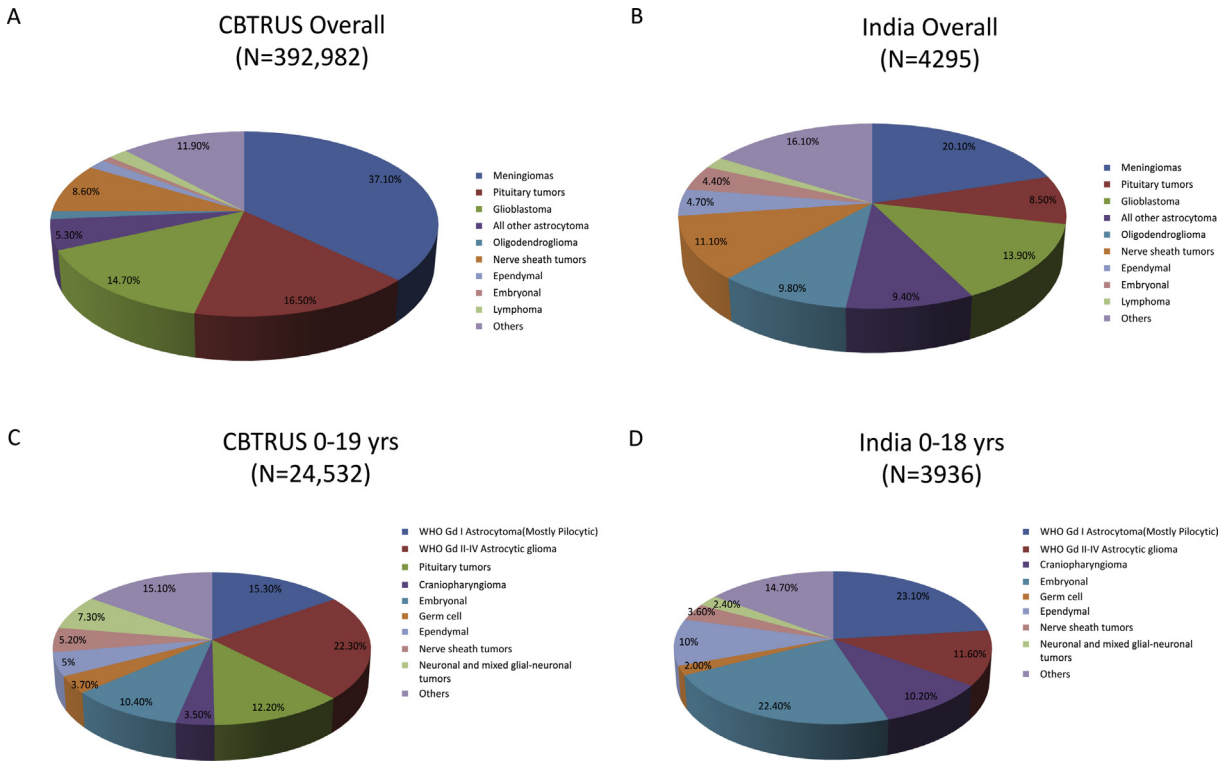

Fig 2. Representative histopathological spectrum of tumours of the brain central nervous system in the overall population (A, B) and in children (C, D) from the West (USA) and the East (India), respectively. USA data are extracted from the Central Brain Tumor Registry of the United States (CBTRUS) statistical report 2011–2015, whereas Indian estimates are from a hospital-based cancer registry for the overall population and multi-institutional pooling of data for childhood brain tumours.

Table 2
Five-year net survival rates with 95% confidence intervals in adults and children with primary tumours of the central nervous system by time period of diagnosis in selected countries from the West and the East (all data were extracted from CONCORD-3 [5])

Country (number of registries covered)	Time period of diagnosis	5-year net survival rates (95% confidence interval) in adults	5-year net survival rates (95% confidence intervals) in children
USA (48 registries)	2000–2004	26.8% (26.5–27.2%)	72.1% (71.1–73.2%)
	2005–2009	35.1% (34.8–35.4%)	76.8% (75.9–77.7%)
	2010–2014	36.5% (36.1–36.8%)	78.2% (77.3–79.2%)
Canada (9 registries)	2000–2004	24.7% (23.4–26.0%)	73.3% (68.2–78.4%)
	2005–2009	29.8% (28.5–31.5%)	72.5% (67.7–77.2%)
	2010–2014	29.9% (28.6–31.1%)	72.7% (68.0–77.4%)
Germany (10 registries)	2000–2004	29.1% (24.8–33.3%)	63.1% (56.0–70.2%)
	2005–2009	27.3% (26.2–28.5%)	67.8% (61.1–74.6%)
	2010–2014	29.6% (28.3–30.9%)	69.5% (61.8–77.2%)
UK (4 registries)	2000–2004	20.6% (20.1–21.2%)	68.4% (66.2–70.7%)
	2005–2009	23.8% (23.3–24.4%)	69.1% (66.9–71.3%)
	2010–2014	26.3% (25.7–26.8%)	71.9% (69.8–74.0%)
India (2 registries)	2000–2004	22.4% (08.3–36.5%)	Not reported
	2005–2009	16.7% (10.4–23.0%)	
	2010–2014	30.0% (17.5–42.6%)	
China (21 registries)	2000–2004	22.7% (20.5–25.0%)	32.7% (21.0–44.4%)
	2005–2009	26.4% (25.2–27.7%)	39.1% (31.2–47.0%)
	2010–2014	32.0% (30.6–33.5%)	41.1% (32.0–50.1%)
Japan (16 registries)	2000–2004	27.9% (26.3–29.5%)	65.3% (59.2–71.5%)
	2005–2009	38.5% (37.2–39.7%)	62.6% (58.1–66.8%)
	2010–2014	46.3% (44.9–47–7%)	69.6% (64.4–74.7%)

recommendations states that the care of all patients with brain and other CNS tumours be co-ordinated through a specific model of multidisciplinary assessment and care with a designated team leader and a clearly defined key worker. Cancer networks should set up robust mechanisms to ensure that every patient with imaging suspicious of a CNS tumour is discussed in a multidisciplinary neuro-oncology clinic. It further recommends timely and efficient provision of diagnostic services (neuropathology and neuroradiology). There should be ready access to neurosurgical services, including image localisation and stereotactic techniques. Preoperative discussions should be undertaken in neuro-oncology multidisciplinary clinics to determine the optimum approach. Following surgery, the cancer networks should ensure prompt specialist oncology consultation for timely initiation of appropriate adjuvant therapy (radiotherapy and/or chemotherapy). Clinical nurse specialists should be core members of the multidisciplinary team and will probably take on the role of key worker, especially in the early stages of clinical care, providing useful information and continuity of care with other healthcare specialists. Healthcare professionals should have face-to-face communication with patients and caregivers at critical points in the care pathway to discuss diagnosis, prognosis, treatment options (including no active treatment) and end-of-life care. Patients should have rapid access to allied healthcare specialists, including neuropsychiatrists, palliative care specialists and rehabilitation experts as and when required. Cancer networks should support, facilitate and encourage the enrolment of patients on clinical trials.

Capacity Building

Although it may not be very easy to set up and establish a comprehensive and integrated neuro-oncology programme aligned to the NICE guidance document [23] at every level, it is even more challenging to sustain and develop it further. One of the major ways of capacity building is through appropriate training and education via specialist training programmes and fellowships to create an adequately trained workforce for the future. In the West, several academic institutes offer structured fellowships in neuro-oncology after the completion of medical degrees. Although neurosurgery and oncology training within developing countries in the East, including India, is largely in accordance with international standards, there exists no formal mechanism for super-specialisation in neuro-oncology, leading to gaps and lacunae in the delivery of neuro-oncological care. Given the time constraints that most clinicians endure across the healthcare spectrum globally, the West has adopted the concept of a specialist nurse practitioner, who is a key healthcare professional that liaises closely with patients and families. In the Eastern part of the world, including India, this concept is still considered alien, with the primary treating clinician in the team being the first contact for patients and caregivers. Specialty-directed nursing training and education in order to align with modern oncological practice is an important component of capacity building. Integration of a clinical nurse specialist in the neuro-oncology team has potential implications of saving the physicians time, professional development of the nursing community and improvement in the quality of care. Although disease-modifying therapies are generally well utilised in cancer care, including neuro-oncology, the integration of palliative and supportive care early in the disease trajectory is often lagging worldwide [24,25]. A recent task force report [26] of the National Cancer Grid of India recommended the institution of early palliative care to further enhance the benefits of cancer-directed treatment. However, the paucity of palliative care specialists, lack of awareness and delayed referral for end-of-life care in neuro-oncology palliative care need to be addressed holistically.

Evidence-Based Guidelines

One of the most notable and laudable contribution from India that has informed neuro-oncology practice globally is high-quality clinical research (level 1 evidence) showing a significant reduction in neurocognitive and neuroendocrine dysfunction in children and young adults with low-grade/benign brain tumours treated with high-precision stereotactic conformal radiotherapy compared with conventional radiotherapy [27]. Such pragmatic randomised trials may be more easily feasible in developing countries (in the East) but can run in parallel in developed countries (in the West) through mutual sharing of clinical research ideas overcoming geopolitical boundaries. The entire global scientific community, including the West, stands to gain from such a co-operation in terms of cost-effectiveness, expedited accrual and improved generalisability, translating into the faster adoption of newer and novel therapies. The East also benefits from improved infrastructure, reduced abandonment, trained human resources, better follow-up and early access to novel technologies. The infrastructure built for clinical research can be used subsequently to provide improved clinical care in resource-poor settings [28]. Another example is evidence-based flowcharts and algorithms [29] for the management of common CNS tumours developed and adopted by the National Cancer Grid of India for uniformity of care. Management algorithms are updated periodically, incorporating new evidence (accounting for resource constraints) to match global best practices. A recent audit [30] of patients treated based on these algorithms is a fair representation of clinical outcomes in contemporary neuro-oncological practice and compares well with previously published international indexed medical literature. In parallel, the Indian Society of Neuro-Oncology is leading an ambitious initiative of developing evidence-based consensus guidelines for the management of common CNS tumours at the national level. Two such national consensus guidelines on medulloblastoma [31] and adult diffuse glioma [32] have been published and were well received by the Indian neuro-oncology community. One of the key features of the Indian Society of Neuro-Oncology guidelines is the division into mandatory requirements or minimum standards that must be followed

strictly and preferable or optional requirements that are to be considered depending upon infrastructure, availability, expertise and costs.

International Twinning and Outreach Programmes

A twinning programme in oncology is a collaborative relationship [33] between a university hospital or cancer programme in a developed economy (high-income country) and a cancer programme/facility in an underdeveloped or developing economy (LMIC). The International Cancer Expert Corps is a network-oriented global partnership that emphasises sustainability and growth through education, training and mentorship metrics to track the progression of the ability of the programmes to deliver high-quality care, with the long-term goal of each programme becoming a regional cancer centre. Twinning programmes are developed in keeping with the mandate of the National Comprehensive Cancer Network to identify treatment at four resource levels – basic, limited, enhanced and maximal – and deliver a tool for healthcare providers to identify treatment options that will provide the best possible outcome at that resource level. This capacity-building strategy facilitates the creation of a sustainable platform for the sharing of best practices and learning from each other through information and technology transfer. The most relevant case example of a successful twinning programme in paediatric neuro-oncology has been the Jordanian–Canadian experience [34], which led to the closing of the survival gap through the implementation of medulloblastoma protocols [35]. More such international twinning programmes between the West and the East would potentially improve neuro-oncology care in the future. The management of cancer in children remains one of the most complex types of medical care to deliver. However, with increasing collaboration and narrowing of the technology gap, developed nations can help substantially improve cancer care in childhood, including paediatric neuro-oncology in LMICs [36,37]. To improve access and care for children and adolescents with cancer, including CNS tumours, the International Society of Pediatric Oncology established a Pediatric Oncology in Developing Countries committee [38] to promote twinning programmes, support key projects in LMICs, set standards for training and care, define the structure and function of paediatric oncology units in resource-constrained environments and provide evidence-based regimen recommendations adapted to the local resource levels [39]. The International Society of Pediatric Oncology has also partnered with the World Health Organization Global Initiative for Childhood Cancer, which aims to reach at least a 60% survival rate for children with cancer (including primary brain tumours) globally by 2030, thereby saving an additional one million lives [40]. The objectives of this Initiative are two-fold: to increase the prioritisation of childhood cancer through raising awareness at global and national levels and to expand the capacity of countries to deliver best practices in childhood cancer care. Concretely, the World Health Organization will support governments to assess current capacities in cancer diagnosis and treatment, including the availability of medicines and technologies; set and cost priority cancer diagnosis and treatment programmes; and integrate childhood cancer into national strategies, health benefits packages and social insurance schemes. The Society for Neuro-Oncology seeks to promote clinical and research activities in neuro-oncology in developing regions in the world through their international outreach mission. Geographical areas have been identified for the purpose of developing outreach programmes tailored to meet the needs of the neuro-oncology community specific to that region, including the provision of educational materials, teaching and training resources, as well as information on international fellowships and funding opportunities.

Conclusions

Tumours of the brain and CNS, although rare, represent a major source of morbidity and mortality worldwide. Globally, there exists substantial variability, with a significantly higher incidence in developed countries compared with developing countries, possibly attributable to differences in environmental and genetic factors as well as resource limitations. Non-uniformity of care with large variations in clinical pathways results in significantly inferior outcomes in many LMICs. Collaboration with the West in establishing comprehensive multidisciplinary neuro-oncology programmes, including the development of care pathways, adoption of evidence-based guidelines and international twinning programmes for capacity building are some of the opportunities that need to be utilised by the East to improve outcomes.

Conflicts of interest

The authors declare no conflict of interest.

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