Epidemiology and Anatomical Distribution of Primary Brain Tumors Among Children in Palestine: A 6-Year National Referral Institution Study

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■ OBJECTIVE: **To investigate the incidence rate of primary brain tumors (PBTs) among Palestinian children over a 6-year interval. This study also aimed to identify the predominant histopathologic types identified in these children.**

■ METHODS: **This retrospective epidemiologic study focused on PBTs in children (<15 years) in Palestine. The data were collected from the registry system at Al-Makassed Hospital in Jerusalem, a prominent referral institution in Palestine and the largest center for PBTs in the region, over a 6 years period from 2018 to 2023.**

■ RESULTS: **The incidence rate of PBTs in children (<15 years) was 1.33 per 100,000 person-years, with a 5% mortality rate. Pilocytic astrocytoma was the most common type (24%), followed by medulloblastoma (15.2%) and glioblastoma (6.3%). About one half of the tumors in children were malignant. Headaches were the most common first sign or symptom. About 20% of brain tumors in children were situated within the ventricles, making it the most prevalent location of these tumors, followed by the cerebellum (15.19%) and frontal lobe (11.39%).**

■ CONCLUSIONS: **This is the first national study in Palestine investigating PBTs in children. The crude incidence rate of primary brain tumors among Palestinian children was lower than the incidence rate in many countries around the world. It is recommended that more research be done on the epidemiology and distribution of PBTs in children in Palestine.**

INTRODUCTION

Primary brain tumors (PBTs) represent the most common category of solid malignancies in childhood,[1] in terms of overall pediatric cancers; they are only second to leukemia.[2] PBTs are dichotomously classified as supratentorial and infratentorial tumors.[3] The 2016 Classification of the World Health Organization (WHO) of Central Nervous System (CNS) tumors involves molecular characteristics along with immunohistology to provide a better understanding of the tumor and its types.[4] PBTs have different classifications and groups, mainly divided into benign and malignant tumors, originating from various regions of the brain such as the skull base, meninges, cranial nerves, and the brain parenchyma.

Despite the conduction of multiple studies to determine the exact risk factor for childhood primary, the exact cause is still unknown; however, genetics and environmental factors might come to blame for the pathogenesis, in addition to some predisposed congenital syndromes that showed an association with certain childhood PBTs.[2] PBTs are caused by a variety of factors, including sex, age, geographic location, race, and ethnicity. In the United States, the reported PBTs and CNS tumors among children and adolescents were 6.06 cases per 100,000 from 2016 to 2020, accounting for 27.9% of malignant cases and 72.1% of

Key words
- Brain
- Children
- Incidence
- Palestine
- Tumors

Abbreviations and Acronyms
CBTRUS: Central Brain Tumor Registry of the United States
CNS: Central nervous system
PBT: Primary brain tumors
WHO: World Health Organization

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them being malignant.[5] Meanwhile, in Canada, 23.4% of cancers diagnosed in children younger than the age of 15 were CNS tumors, which were the leading cause of mortality and morbidity in the same age group.[6]

The most common histopathologic type of childhood primary brain tumor in the United States has been counted as glioma, with the most common malignant type being the glioblastoma (14.2% of all tumors and 50.9% of all malignant tumors), and the most common nonmalignant type was meningioma (40.8% of all tumors and 56.2% of all nonmalignant tumors). In addition, female children were affected more than male children with childhood PBT (6.27 vs. 6.00 per 100,000).[5]

PBTs can present with various features in children and adolescents, ranging from headache (41%), vomiting (12%), unsteadiness (11%), visual difficulties (10%), educational or behavioral problems (10%), and seizures (9%), with a median interval for the presenting symptoms being 2.5 months; moreover, the shorter the symptom interval, the more it was associated with high-grade tumors and patient age of 3 years or younger.[7]

Epidemiologic studies play a vital role in providing clinicians with accurate and up-to-date information to assist patients and families dealing with this common clinical entity. We conducted a literature review on numerous databases, including PubMed and Scopus, and we were unable to find any recent articles on the epidemiology or characteristics of childhood PBTs in Palestine which were even lacking in the annual report of the Palestinian Ministry of Health. This indicates that data on the epidemiology and anatomical distribution of PBTs in adults in Palestine is hard to come by. The goal of this study was to look at the incidence rate of childhood PBTs in Palestine across the last 6 years (2018–2023), as well as their epidemiologic characteristics, histologic types, and anatomical distribution.

METHODS

Study Design and Setting

The study design was a retrospective, descriptive, epidemiologic study. The data were collected from clinical reports, histopathology reports, and radiology reports at Al-Makassed Hospital in Jerusalem, the largest referral center for PBTs in Palestine. The data were collected from reports for children (<15 years) diagnosed with PBTs and referred to Al-Makassed Hospital for treatment in the period from 2018 to 2023. The use of the <15 years old cut off stems from various factors. First, it aligns with the homogeneity observed in primary brain tumor types among children in this age group. Second, there are limitations on referrals for individuals older than 14 years old from Gaza Strip to Jerusalem. Lastly, the Palestinian Central Bureau of Statistics lacks specific data on population sizes for ages 0–18 years, hindering the calculation of incidence rates for pediatric brain tumors. In addition, this age cut-off has been adopted in study conducted in Britain.[8] Our target population was Palestinian children <15 years diagnosed with PBTs and treated at Al-Makassed Hospital in Jerusalem during this period.

Inclusion and Exclusion Criteria

Palestinian patients aged from 0 to 14 years with PBTs referred to or diagnosed at Al-Makassed Hospital were included in this study. Patients >14 years old, patients with secondary (metastatic) brain tumors, and patients with spinal cord tumors were excluded from the study.

Study Variables

Age at time of diagnosis (<15 years), sex (either male or female), place of residency (West Bank or Gaza Strip), and type of residency (city, village, or refugee camps) were the sociodemographic variables included in this study. The variables for the clinical data included in this study were the type of the tumor stated in the histopathology report, behavior of the tumor (0; benign, 1; unspecified, borderline, or uncertain behavior, 2; carcinoma in situ and grade III intraepithelial neoplasia, 3; malignant), based on the 2016 WHO Classification for CNS tumors,[9] and anatomical location within the brain based on the second revision of the third edition of the *International Classification of Diseases of Oncology* manual.[10] The reason behind using 2016 WHO Classification for CNS tumors instead of the recent update of the Classification in 2021 is that the updated version depends on the molecular studies which are not done at Al-Makassed Hospital due to financial reasons. In addition, we reviewed reports for patients from 2018 to 2020, in which the 2021's version was not already published; therefore, the reports of these patients did not include the diagnosis based on the molecular studies.

Data Collection and Tool

The sociodemographic data were collected from the clinical reports of the patients. The clinical data including the type of the tumor and anatomical location were collected from the histopathology and radiology reports. The reports were obtained from the registry system at Al-Makassed Hospital and returned to the hospital after the completion of the study. The publications of the Palestinian Central Bureau of Statistics were used to obtain the population size (<15 years) for each year from 2018 to 2023. The annual crude incidence rate was calculated based on the population size for each year.

Ethical Consideration

The Palestinian Ministry of Health and the An-Najah National University Institutional Review Board provided ethical approval for this study. During this study, no patient-identifiable information was collected. The clinical, histopathologic, and radiologic reports were returned to Al-Makassed Hospital when this study was concluded.

Data Analysis

The Statistical Package for Social Sciences (SPSS) version 26.0, from IBM Corp. (Armonk, New York, USA) was used for the statistical analysis. Descriptive statistical analysis was conducted for continuous and categorical variables, means, standard deviations, frequency, and percentages were calculated and reported. Inferential analysis with cross-tabulation and χ^2 test was used to analyze the categorical variables. Any P values <0.05 were considered statistically significant, with a 5% level for statistical significance.

Table 1. Sociodemographic Characteristics of Patients

Variable	Frequency (*n*)/Mean	Percentage (%)/SD
Age at diagnosis, years, mean	7.46	(±3.83)
Sex		
Male	77	48.7
Female	81	51.3
Type of residency		
City	82	51.9
Village	65	41.1
Refugee camps	11	7
Place of residency		
West Bank	70	44.3
Gaza Strip	88	55.7
Total	158	100

SD, standard deviation.

RESULTS

Sociodemographic Characteristics of Patients

Among the 158 patients aged ≤14 years diagnosed with PBTs over the period from 2018 to 2023, 51.3% were female and 48.7% were male. The mean age at diagnosis for those patients was 7.46 years (±3.83 years). Around 56% of the patients were from the Gaza Strip, and 44% were from the West Bank. Approximately, 52% of the patients lived in the major cities, 41% lived in villages, and only 7% were from the refugee camps. The sociodemographic characteristics of the patients are presented in Table 1.

Epidemiology of PBTs in Children (<15 Years)

The annual incidence rate of PBTs in Palestinian children (<15 years) during the period from 2018 to 2023 ranged from 1.12 to 1.46 per 100,000 person-years, with an average annual incidence of 1.33 per 100,000 person-years. For male children, the annual incidence rate ranged from 0.85 to 1.66 per 100,000 person-years, with an average annual incidence of 1.27 per 100,000 person-years. The annual incidence rate for female children ranged from 0.94 to 2.08 per 100,000 person-years, with an average annual incidence of 1.39 per 100,000 person-years. The male-to-female ratio for the average annual incidence rate was 1:1.09 (0.92). The annual incidence rates for patients (<15 years) are presented in Table 2 and illustrated in Figure 1.

Mortality

In children (<15 years), primary brain tumors had a 5% overall mortality rate. No statistically significant differences in mortality were found between the groups based on gender, the behavior of the tumor, type of residency, and place of residency ($P = 0.941$, 0.486, 0.686, and 0.691, respectively). Choroid plexus carcinoma, medulloblastoma not otherwise specified, and germinoma were the most common tumors associated with a high mortality rate (100%, 50%, and 33.3%, respectively) but the results were not statistically significant ($P = 0.219$). Regarding the type of treatment associated with mortality, gross total resection alone was the only modality of treatment associated with mortality (5.7%), but the results were not statistically significant ($P = 0.971$). The relationship between the type of tumors and mortality and modality of treatment is shown in the Supplementary Tables 1 and 2, respectively.

First Signs or Symptoms of PBTs

Headaches (33%), focal signs (motor and sensory) (27%), and seizures (19%) were the most common first presenting signs or symptoms of PBTs in children (<15 years). Of the patients who presented with headaches as their first symptoms, 48.1% of them were diagnosed with a malignant tumor, 40.4% of them were diagnosed with a borderline tumor, and only 11.5% were diagnosed with a benign tumor ($P = 0.015$). Malignant tumors were diagnosed in 70.8% of patients who presented with nausea, vomiting, or dizziness as their first symptom. The first signs/symptoms of PBTs are presented in Table 3.

Table 2. Annual Incidence Rates for PBTs in Patients (<15 Years) by Gender

Year	Number of Cases	Population Size	Crude Incidence Rate*	Male Population Size	Incidence Rate in Male Patients*	Female Population Size	Incidence Rate in Female Patients*	Male:Female Ratio
2018	25	1,894,822	1.32	970,349	1.55	942,473	1.06	1.46:1
2019	28	1,930,066	1.45	987,823	1.11	942,243	1.80	1:1.62
2020	22	1,963,697	1.12	1,004,623	1.29	959,355	0.94	1.38:1
2021	30	1,997,890	1.50	1,021,423	1.66	976,467	1.33	1.25:1
2022	23	2,030,211	1.13	1,037,391	1.16	992,820	1.11	1.04:1
2023	30	2,061,521	1.46	1,052,825	0.85	1,008,696	2.08	1:2.45
Average	—	—	1.33	—	1.27	—	1.39	1:1.09

*Per 100,000.

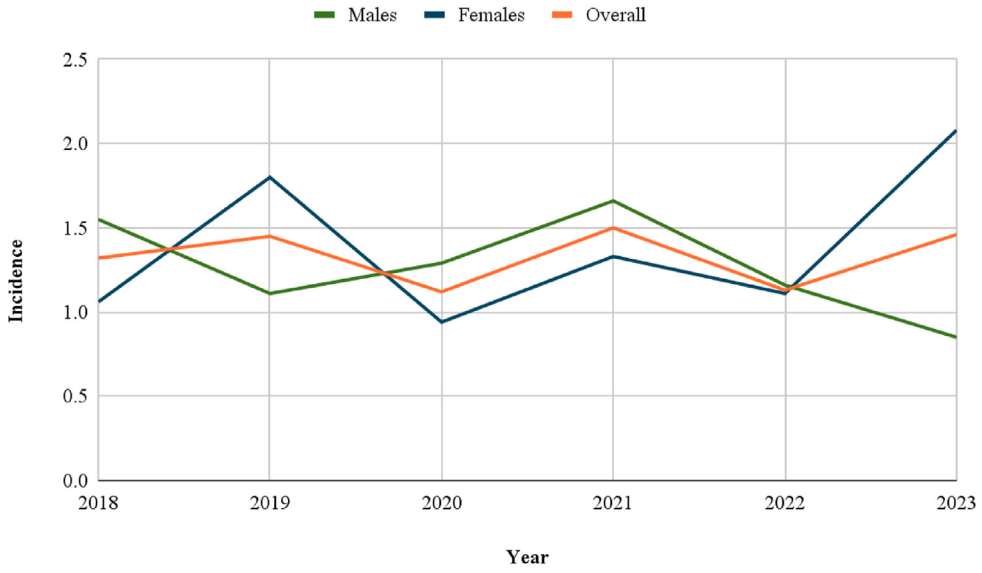

Figure 1. Incidence rate of primary brain tumors in children (<15 years) per 100,000 population.

Histopathologic Types of PBTs in Children (<15 Years Old)

Overall, 34 histopathologic types of PBTs were identified in children (<15 years) in Palestine from 2018 to 2023. Other astrocytic tumors (25.3%), embryonal tumors (22.2%), and diffuse astrocytic and oligodendroglial tumors (13.3%) were the most common histology groups in our study. Tumors of the cranial and paraspinal nerves (0.6%) were our cohort's least common histology group. Pilocytic astrocytoma (24%), classic type of medulloblastoma (15.2%), and glioblastoma (6.3%) were the most common histopathologic types identified. The average annual incidence rate of pilocytic astrocytoma was 0.31 per 100,000 person-years, and for the classic type of medulloblastoma was 0.20 per 100,000 person-years. No significant differences in the rates for the types of tumors between boys and girls were identified ($P = 0.199$). The histologic types of PBTs in children (<15 years) are presented in Table 4 and illustrated in Figure 2.

Behavior of the Tumors

Malignant tumors constituted about 50% of the PBTs in children (<15 years). Unspecified, borderline, or tumors with uncertain behavior were 36.1%, and benign tumors were only 13.9% of the PBTs in this age group. The average annual incidence for

Table 3. First Signs/Symptoms of PBTs in Children (<15 Years)

First Sign/Symptom	Total, *n* (%)	Benign	Unspecified, Borderline, or Uncertain Behavior	Malignant	*P* Value
Headache	52 (33)	6 (11.5)	21 (40.4)	25 (48.1)	0.015
Focal signs (motor or sensory signs)	43 (27)	5 (11.6)	18 (41.9)	20 (46.5)	
Seizure	30 (19)	10 (33.3)	10 (33.3)	10 (33.3)	
Nausea/vomiting/dizziness	24 (15)	0 (0)	7 (29.2)	17 (70.8)	
Mental status alteration (drowsiness, confusion, etc.)	6 (4)	0 (0)	1 (16.7)	5 (83.3)	
Cognitive and emotional dysfunction	1 (1)	0 (0)	0 (0)	1 (100)	
Dysarthria	1 (1)	1 (100)	0 (0)	0 (0)	
Neurogenic bladder/bowel	1 (1)	0 (0)	0 (0)	1 (100)	
Total	158	22 (13.9)	57 (36.1)	79 (50)	

PBT, primary brain tumor.

Table 4. Histopathologic Types of PBTs in Children (<15 Years Old)

Type	Code	Female (%)	IR	Male (%)	IR	Total (%)	IR
Diffuse astrocytic and oligodendroglial tumors		10 (52.4)	0.17	11 (47.6)	0.18	21 (13.3)	0.18
Gemistocytic astrocytoma	9411/3	0 (0)	0	1 (100)	0.02	1 (0.6)	0.01
Anaplastic astrocytoma	9401/3	4 (100)	0.07	0 (0)	0	4 (2.5)	0.03
Glioblastoma	9440/3	3 (30)	0.05	7 (70)	0.11	10 (6.3)	0.08
Diffuse low-grade glioma	9452/1	0 (0)	0	1 (100)	0.02	1 (0.6)	0.01
Diffuse midline glioma	9385/3	0 (0)	0	1 (100)	0.02	1 (0.6)	0.01
Oligodendrogliomas	9450/3	3 (75)	0.05	1 (25)	0.02	4 (2.5)	0.034
Other astrocytic tumors		25 (55.6)	0.41	15 (44.4)	0.25	40 (25.3)	0.33
Pilocytic astrocytoma	9421/1	24 (63.2)	0.39	14 (36.8)	0.23	38 (24)	0.31
Subependymal giant cell astrocytoma	9384/1	1 (50)	0.02	1 (50)	0.02	2 (1.3)	0.017
Ependymal tumors		6 (50)	0.1	6 (50)	0.1	12 (7.8)	0.1
Ependymoma	9391/3	4 (66.7)	0.07	2 (33.3)	0.03	6 (3.9)	0.05
Anaplastic ependymoma	9392/3	2 (33.3)	0.03	4 (66.7)	0.07	6 (3.9)	0.05
Other gliomas		2 (100)	0.03	0 (0)	0	2 (1.3)	0.016
Astroblastoma	9430/3	2 (100)	0.03	0 (0)	0	2 (1.3)	0.016
Choroid plexus tumors		1 (50)	0.02	1 (50)	0.02	2 (1.3)	0.017
Choroid plexus papilloma	9390/0	1 (100)	0.02	0 (0)	0	1 (0.6)	0.008
Choroid plexus carcinoma	9390/3	0 (0)	0	1 (100)	0.02	1 (0.6)	0.008
Neuronal and mixed neuronal-glial tumors		5 (35.7)	0.08	9 (64.3)	0.15	14 (9)	0.117
Dysembryoplastic neuroepithelial tumor	9413/0	2 (33.3)	0.03	4 (66.7)	0.07	6 (3.9)	0.05
Ganglioglioma	9505/1	2 (33.3)	0.03	4 (66.7)	0.07	6 (3.9)	0.05
Anaplastic ganglioglioma	9505/3	1 (100)	0.02	0 (0)	0	1 (0.6)	0.008
Desmoplastic infantile astrocytoma and ganglioglioma	9412/1	0 (0)	0	1 (100)	0.02	1 (0.6)	0.009
Embryonal tumors		18 (51.4)	0.31	17 (48.6)	0.28	35 (22.2)	0.296
Medulloblastoma, classic	9470/3	12 (50)	0.21	12 (50)	0.20	24 (15.2)	0.20
Medulloblastoma, desmoplastic/nodular	9471/3	1 (33.3)	0.02	2 (66.7)	0.03	3 (1.9)	0.026
Medulloblastoma, large cell/anaplastic	9474/3	2 (100)	0.03	0 (0)	0	2 (1.3)	0.017
Medulloblastoma, NOS	9470/3	2 (100)	0.04	0 (0)	0	2 (1.3)	0.017
Embryonal tumor with multilayered rosettes	9478/3	1 (100)	0.02	0 (0)	0	1 (0.6)	0.008
Atypical teratoid/rhabdoid tumor	9508/3	0 (0)	0	3 (100)	0.05	3 (1.9)	0.025
Tumors of the cranial and paraspinal nerves		0 (0)	0	1 (100)	0.02	1 (0.6)	0.008
Cellular schwannoma	9560/0	0 (0)	0	1 (100)	0.02	1 (0.6)	0.008
Meningiomas		2 (66.7)	0.03	1 (33.3)	0.02	3 (1.9)	0.025
Meningioma	9530/0	0 (0)	0	1 (100)	0.02	1 (0.6)	0.008
Atypical meningioma	9539/1	2 (100)	0.03	0 (0)	0	2 (1.3)	0.017
Mesenchymal, non-meningothelial tumors		5 (41.7)	0.08	7 (58.3)	0.11	12 (7.6)	0.10
Hemangioma	9120/0	4 (50)	0.07	4 (50)	0.07	8 (5)	0.066
Fibrosarcoma	8810/3	1 (50)	0.02	1 (50)	0.02	2 (1.3)	0.016

NOS, not otherwise specified; IR, incidence rate; PBT, primary brain tumor.

Continues

Table 4. Continued

Type	Code	Female (%)	IR	Male (%)	IR	Total (%)	IR
Rhabdomyosarcoma	8900/3	0 (0)	0	2 (100)	0.03	2 (1.3)	0.017
Histiocytic tumors		2 (100)	0.03	0 (0)	0	2 (1.3)	0.016
Juvenile xanthogranuloma	9750/1	2 (100)	0.03	0 (0)	0	2 (1.3)	0.016
Germ cell tumors		1 (25)	0.02	3 (75)	0.05	4 (2.5)	0.034
Germinoma	9064/3	1 (33.3)	0.02	2 (66.7)	0.03	3 (1.9)	0.026
Immature teratoma	9080/3	0 (0)	0	1 (100)	0.02	1 (0.6)	0.008
Tumors of the sellar region		4 (40)	0.07	6 (60)	0.10	10 (6.3)	0.085
Pituitary adenoma	8040/0	0 (0)	0	1 (100)	0.02	1 (0.6)	0.009
Craniopharyngioma	9350/1	4 (44.5)	0.07	5 (55.5)	0.08	9 (5.7)	0.076
Total		81 (51.3)	1.39	77 (48.7)	1.27	158	1.33

NOS, not otherwise specified; IR, incidence rate; PBT, primary brain tumor.

nonmalignant tumors (benign and borderline tumors) was 0.66 per 100,000 person-years, and the average annual incidence for malignant tumors was 0.67 per 100,000 person-years. No significant differences in the percentage of malignant, benign, and borderline tumors among the different groups based on gender, type of residency, and place of residency (*P*-values 0.621, 0.405, and 0.125 respectively). The distribution of tumors based on the behavior in the different groups is presented in Table 5.

Anatomical Location of PBTs

The ventricles (20.25%), cerebellum (15.19%), frontal lobe (11.39%), and brain stem (10.13%) were the most common sites for PBTs in children (<15 years). The occipital lobe (1.27%) and pineal gland (1.27%) were the least common sites for PBTs. The most common anatomical locations for malignant tumors were the ventricles (31.6%), cerebellum (15.2%), and the cerebrum (11.4%). The cerebellum (19.3%), craniopharyngeal duct (15.8%), and brain stem (14%) were the most common anatomical locations for unspecified, borderline, or tumors with uncertain behavior. For benign tumors, the most common location was the frontal lobe (36.4%). The anatomical locations of PBTs are shown in Table 6 and illustrated in Figure 3.

DISCUSSION

During past decades, the incidence of PBTs in many countries around the world has increased, resulting from the emergence and

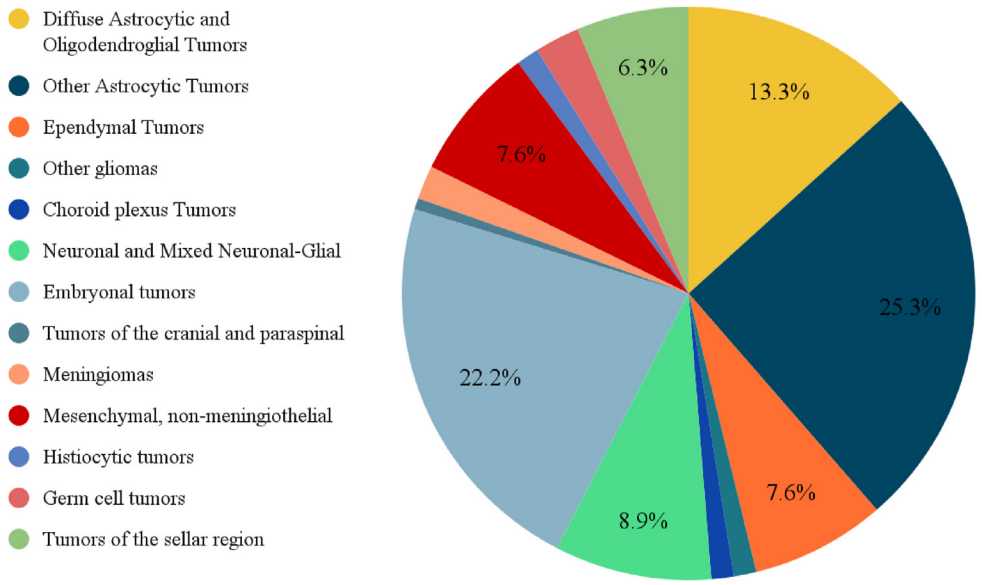

Figure 2. Histology groups of primary brain tumor types in children (<15 years).

Table 5. The Distribution of PBTs Based on the Behavior in the Different Groups

Variable	Benign, *n* (%)	Unspecified, Borderline, or Uncertain Behavior, *n* (%)	Malignant, *n* (%)	*P* Value
Sex				
Male	12 (15.6)	25 (32.5)	40 (51.9)	0.621
Female	10 (12.4)	32 (39.5)	39 (48.1)	
Type of residency				
City	11 (13.4)	26 (31.7)	45 (54.9)	0.405
Village	11 (16.9)	26 (40)	28 (43.1)	
Refugee Camp	0 (0)	5 (45.5)	6 (54.5)	
Place of residency				
West Bank	14 (20)	25 (35.7)	31 (44.3)	0.125
Gaza Strip	8 (9.1)	32 (36.4)	48 (54.5)	
Total	22 (13.9)	57 (36.1)	79 (50)	

PBT, primary brain tumor.

use of new imaging modalities.[11,12] The epidemiology of PBTs, distribution of histopathologic types, and anatomical locations were investigated in this study.

The crude incidence rate of PBTs in Palestinian children (1.33 per 100,000 person-years) is lower than the incidence rate of PBTs in children from other countries around the world, including Canada (3.57 per 100,000 person-years),[6] and United States (6.13 per 100,000 person-years).[5] Our crude incidence rate could be attributed to various factors, including the involvement of patients from a single referral center in Palestine. In addition,

Table 6. Anatomical Locations of PBTs in Children (<15 Years) According to the ICD-O-3

Site	ICD-O-3 Site Code	*n*	(%)	Benign	Unspecified, Borderline, or Uncertain Behavior	Malignant	*P* Value
Cerebrum	C71.0	13	8.23	0 (0)	4 (30.8)	9 (69.2)	<0.001
Frontal lobe	C71.1	18	11.39	8 (44.5)	4 (22.2)	6 (33.3)	
Temporal lobe	C71.2	12	7.59	3 (25)	6 (50)	3 (25)	
Parietal lobe	C71.3	10	6.33	2 (20)	0 (0)	8 (80)	
Occipital lobe	C71.4	2	1.27	0 (0)	2 (100)	0 (0)	
Ventricle	C71.5	32	20.25	1 (3.1)	6 (18.8)	25 (78.1)	
Cerebellum	C71.6	24	15.19	1 (4.2)	11 (45.8)	12 (50)	
Brain stem	C71.7	16	10.13	2 (12.5)	8 (50)	6 (37.5)	
Other brain							
Overlapping lesion of brain	C71.8	5	3.16	1 (20)	1 (20)	3 (60)	
Brain, NOS	C71.9	5	3.16	2 (40)	1 (20)	2 (40)	
Cerebral meninges	C70.0	5	3.16	1 (20)	2 (40)	2 (40)	
Pituitary and craniopharyngeal duct							
Pituitary gland	C75.1	5	3.16	1 (20)	3 (60)	1 (20)	
Craniopharyngeal duct	C75.2	9	5.70	0 (0)	9 (100)	0 (0)	
Pineal gland	C75.3	2	1.27	0 (0)	0 (0)	2 (100)	

ICD-O-3, *International Classification of Diseases for Oncology, Third Edition*; NOS, not otherwise specified; PBT, primary brain tumor.

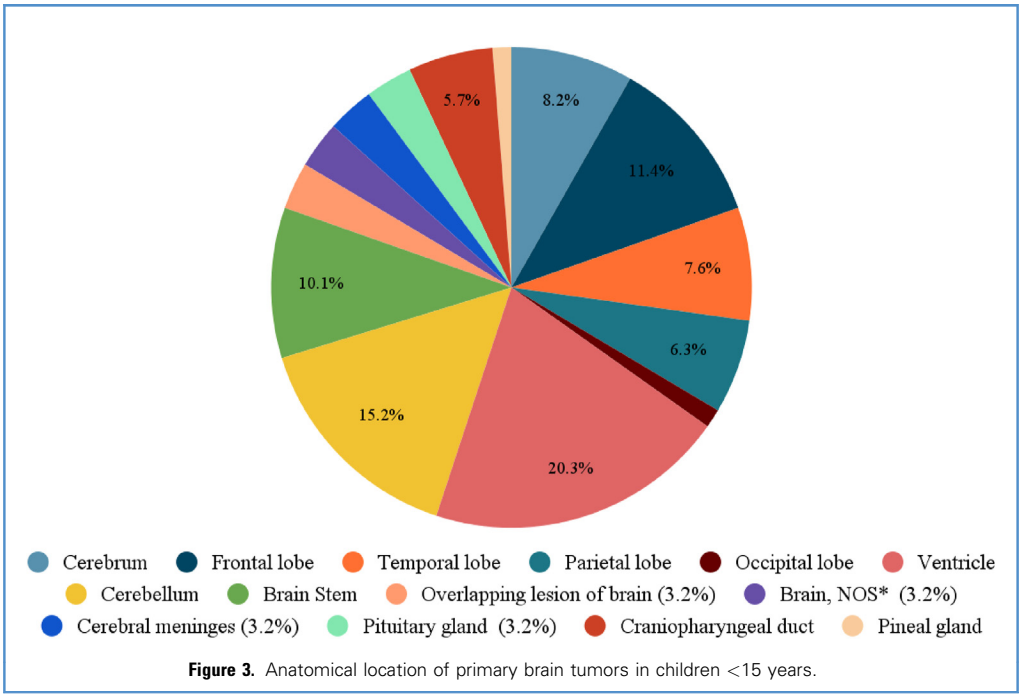

Figure 3. Anatomical location of primary brain tumors in children <15 years.

the health care system in Palestine faces some challenges, particularly in the lack of clinical referral centers, especially for patients from Gaza strip and even from West Bank. Furthermore, some patients are referred to health care facilities outside of Palestine, such as neighboring countries like Jordan.

A study conducted among patients younger than 20 years old with primary brain tumors of in Jordan found that the crude incidence rate was (2.09 per 100,000).[13] The incidence rate was slightly greater in female patients than male patients, which was consistent with the results of other previous studies from the United States.[5,14] In contrast, the male-to-female ratio in our study was lower than the ratio reported in the recent study in Jordan (0.92 vs. 1.77).[13]

No specific trends in the annual incidence rates from 2018 to 2023 were observed. In our study, there was no difference in the average annual incidence rate for malignant and nonmalignant tumors (0.67 and 0.66, respectively). The incidence rate for malignant tumors in Palestinian children was lower than the incidence rate for malignant tumors in children in the United States reported in the recent Central Brain Tumor Registry of the United States (CBTRUS) report (3.42 per 100,000 person-years).[5]

Of the 158 patients diagnosed with a primary brain tumor from 2018 to 2023, only 8 patients died (5%). According to the most recent report from CBTRUS, brain and CNS tumors in children <15 years significantly contribute to cancer-related deaths, and it is the leading cause of cancer deaths in this age group.[5] We did not find any significant association between mortality and behavior of the tumor ($P = 0.486$), or between mortality and sociodemographic variables such as gender, type, or place of residency.

The most common first signs or symptoms of PBTs in children <15 years were headache, focal signs (motor and sensory), and seizures. Other signs and symptoms of the first presentation were consistent with the signs and symptoms of increased intracranial pressure. These results were consistent with the findings of a recent study in a center in the Western Province of Saudi Arabia.[15] Interestingly, about 83% of the patients presented with mental status alternation were diagnosed with a malignant tumor ($P = 0.015$). About 50% of the tumors identified in children (<15 years) were malignant. In Lebanon, the ratio of malignant to nonmalignant tumors in children was 4.06.[16] We did not observe any significant differences in the behavior of the tumors in relation to gender, type, or place of residency.

The most common histology group of tumors in children identified in our study was the other astrocytic tumors. This finding was similar to the findings from the recent report of the CBTRUS, in which the "other astrocytic tumors" were the most common group of tumors identified in children 0–14 years, with an incidence rate of 1.23 per 100,000 person-years,[5] compared with a rate of 0.33 per 100,000 person-years identified in our study. Although the embryonal tumors group was the most common histology group identified in Lebanese children,[16] it was the second most common histology group identified in our study, with the diffuse astrocytic and oligodendroglial tumors coming third in the list. Pilocytic astrocytoma was the most common histopathologic type of primary brain tumor identified in Palestinian children. This finding aligns with previous studies conducted in Austria involving patients younger than 18 years old,[17] as well as studies in the United States focusing on patients aged 14 years and younger.[5,14] The incidence rate of

pilocytic astrocytoma in children was slightly greater in female children than in male children, but this finding was not statistically significant. A previous study in Korea showed that the incidence rate of pilocytic astrocytoma was significantly greater in female children compared to males.[18] In Lebanese children, medulloblastoma was the most common histopathologic type identified,[16] while medulloblastoma (classic type) was the second most common type identified in Palestinian children.

For the anatomical locations of PBTs in Palestinian children, the most common locations were the ventricles, cerebellum, frontal lobe, and brain stem. CBTRUS's most recent report showed that the most common anatomical locations of PBTs in children from the first to the third were the cerebellum, other brain (C71.8 and C71.9), and brain stem, respectively.[5] In Lebanese children, the most common anatomical locations of PBTs were other brain (C71.8 and C71.9), cerebellum, and cerebral meninges.[16]

One of the limitations of this study is the lack of data from previous studies on the epidemiology of PBTs in Palestinian children before 2018, which did not enable us to compare the types of PBTs or the annual incidence rates before this period with the results of our study. Second, we only collected the data from Al-Makassed Hospital in Jerusalem, and we could not collect the data from all of the hospitals that receive Palestinian patients with PBTs, as some of the Palestinian patients are unable to obtain the permission to enter Jerusalem or are referred to other hospitals outside of Palestine, which may have caused a selection bias, as the sample of our study does not contain all of the Palestinian patients with PBTs during the period from 2018 to 2023. Another limitation is that the referral of oncology cases including the cases of PBTs to Al-Makassed Hospital stopped after October 2023. Therefore, the number of cases and annual incidence rate in 2023 may not be accurate.

This study has many strengths. First, it is the first study of PBTs in Palestinian children, including epidemiology, types, and anatomical locations. Second, the data were collected from Al-Makassed Hospital in Jerusalem, which is the largest referral center in Palestine for PBTs; therefore, the results of our study can be safely generalized to the Palestinian children with PBTs. In addition, the registry system at Al-Makassed Hospital contained all the data required to meet the objectives of the study, with no missing data. Finally, the results of this study can be a valuable addition to the resources of the Annual Health Reports of the Palestinian Ministry of Health.

We recommend using the methodology used in our study in future studies that tackle the epidemiology, types of PBTs, and anatomical location of tumors to facilitate the comparison between the results of studies from different areas around the world and facilitate the generation of systematic reviews on this topic. We encourage conducting more research studies on the epidemiology, types of PBTs, and anatomical locations in Palestinian children to ensure the availability of information on PBTs in Palestinian children in the upcoming years.

CONCLUSIONS

This is the first study of primary brain tumor types, anatomical location, and epidemiology in Palestinian children. The crude incidence rate of primary brain tumors in children (<15 years) was 1.33 per 100,000 person-years, lower than the incidence rate in many countries around the world, with a male-to-female ratio of 0.92. Pilocytic astrocytoma was the most common histopathologic type identified in Palestinian children with an incidence rate of 0.31 per 100,000 person-years. The most common anatomical location for PBTs in Palestinian children was the ventricles (C71.5). The most common first symptom of PBTs in children was headache. Using a similar methodology to generate future studies on the same topic is recommended to provide constant information on brain tumors in Palestinian children.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Ahmad Rjoub: Writing — review & editing, Writing — original draft, Visualization, Validation, Methodology, Formal analysis, Data curation. **Wafaa Abu Zahra:** Writing — review & editing, Writing — original draft, Visualization, Methodology, Formal analysis, Data curation. **Noor Issa:** Writing — review & editing, Writing — original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Yazan Dumaidi:** Writing — review & editing, Writing — original draft, Visualization, Methodology, Formal analysis, Data curation. **Mohammad Abuawad:** Writing — review & editing, Writing — original draft, Visualization, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ahmed Daqour:** Writing — review & editing, Writing — original draft, Visualization, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Abdulsalam Alkaiyat:** Writing — review & editing, Writing — original draft, Visualization, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Shahed Nasser:** Writing — original draft, Visualization, Methodology, Data curation.

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Upon reasonable request for the corresponding author, the data of this study are available.

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SUPPLEMENTARY DATA

Supplementary Table 1. Histopathologic Types of Primary Brain Tumors Associated with Mortality

Type of Tumor	Alive	Deceased	*P* Value*
Pilocytic astrocytoma	35 (92%)	3 (8%)	0.219
Medulloblastoma, classic	23 (95.9%)	1 (4.1%)	
Ependymoma	5 (83.3%)	1 (16.7%)	
Germinoma	2 (66.7%)	1 (33.3%)	
Medulloblastoma, NOS	1 (50%)	1 (50%)	
Choroid plexus carcinoma	0 (0%)	1 (100%)	

NOS, not otherwise specified.
*χ^2 test.

Supplementary Table 2. Mortality Rate Based on the Type of Treatment in Children with Primary Brain Tumors

Type of Treatment	Alive	Deceased	*P* Value*
Surgery	135 (94.4%)	8 (5.6%)	0.971
Surgery and chemotherapy	3 (100%)	0 (0%)	
Surgery and radiotherapy	5 (100%)	0 (0%)	
Surgery, chemotherapy, and radiotherapy	4 (100%)	0 (0%)	
Chemotherapy	2 (100%)	0 (0%)	
Radiotherapy	1 (100%)	0 (0%)	
Total	150 (95%)	8 (5%)	

Type of surgery: gross total resection.
*χ^2 test.