Epidemiological Trends of Central Nervous System Neoplasms in Saudi Arabia: A Retrospective Analysis Over Three Decades

Kholoud S. Almasoudi[1, 2], Arwa F. Flemban[3*], Saeed M. Kabrah[4], Samah A. Alharbi[5], Hanaa Alahmadi[3], Hanan M. Abd Elmoneim[3, 5, 6], Ruba O. Almaghrabi[7], Asim A. Khogeer[8, 9], Abdullah K. Bahakim[10], Sanad M. Alharthi[10], Saad M. Alharthi[10], Saad F. Alqahtani[10]

[1]Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, University of Tabouk, Saudi Arabia. [2]Prince Fahad bin Sultan Chair for Biomedical Research, University of Tabouk, Saudi Arabia. [3]Department of Pathology, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia. [4]Department of Clinical Laboratory Sciences, Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Saudi Arabia. [5]Department of Physiology, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia. [6]Department of Pathology, Faculty of Medicine, Minia University, Egypt. [7]Department of Laboratory Medicine, Faculty of Applied Medical Sciences, Albaha University, Albaha, Saudi Arabia. [8]Department of Research, The Strategic Planning General Directorate of Health Affairs, Makkah Region, Ministry of Health, Saudi Arabia. [9]Medical Genetics Unit, Maternity & Children Hospital, Makkah, Healthcare Cluster, Ministry of Health, Makkah, Saudi Arabia. [10]Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia.

Abstract

This retrospective study comprehensively analyses the epidemiological trends of Central Nervous System (CNS) cancers in Saudi Arabia over three decades, from 1990 to 2019. Utilizing data from the Institute for Health Metrics and Evaluation (IHME) and the Saudi Cancer Registry, the study examines incidence, prevalence, and mortality rates, offering a detailed depiction of CNS cancer trends in the region. The findings reveal a significant increase in the incidence of CNS cancers, with rates increasing from 1.1 to 3.63 per 100,000 population. Despite this rise, the incidence in Saudi Arabia remains lower than in more developed regions, suggesting regional variations in risk factors and healthcare practices. The study observes a marked decline in mortality rates, from 25% in 1990 to below 10% in 2019, indicative of the effect of advancements in early detection, molecular diagnostics, and therapeutic interventions. Gender disparities were apparent, with males exhibiting higher incidence and mortality rates, aligning with global epidemiological patterns. The study also highlights demographic variability in CNS cancer incidence, with a prominent increase in adult populations, particularly those aged 55 and above. These findings underscore the need for targeted public health strategies and healthcare policies to address the rising incidence and improve patient outcomes. The study advocates for future research focusing on the etiology of CNS cancers, particularly in genetic and environmental factors, and calls for international collaboration in research to understand global variations in CNS cancer trends.

Keywords: CNS cancers, Epidemiology, Incidence rates, Mortality, Public health policy

INTRODUCTION

Epidemiological Overview of CNS Neoplasms Prevalence and Impact of CNS Malignancies

Central nervous system (CNS) cancers, encompassing malignancies of the brain and spinal cord, represent a critical public health concern due to their high morbidity and mortality rates [1, 2]. These neoplasms, accounting for approximately 3.7% of all cancers in men and 2.3% in women, are among the leading causes of cancer-related deaths across various age groups [3]. CNS tumors, particularly brain neoplasms, are the predominant cause of cancer-related mortality in pediatric populations and rank third in adult demographics [4]. Despite advancements in oncological therapies, CNS cancers pose significant challenges due to their heterogeneity, aggressive nature, and complex pathophysiology [5].

Global Incidence and Mortality Patterns of CNS Cancers

Advances in diagnostic modalities, particularly molecular diagnostics, have revolutionized the accuracy of CNS tumor

Address for correspondence: Arwa F. Flemban, Department of Pathology, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia. aflemban@uqu.edu.sa

characterization, emphasizing the role of histopathological classification in treatment planning and prognosis determination [6]. Even benign CNS tumors have deleterious effects, potentially leading to fatal outcomes due to their intracranial location, space-occupying characteristics, and potential for malignant transformation [7]. Notably, the incidence and mortality rates of CNS neoplasms are disproportionately higher in developed regions such as Europe, Australia/New Zealand, and North America, compared to Africa and the Pacific [8].

A critical analysis of age-specific incidence rates is essential in investigating demographic variability in CNS cancer incidence. Such analysis explains the demographic trends and shifts in CNS cancer cases, providing valuable insights into the epidemiology of these malignancies [9, 10]. The incidence of central nervous system (CNS) cancers exhibits notable demographic variability, mainly when analyzed across different age groups. CNS tumors are a significant cause of morbidity and mortality among children [11]. In contrast, adults, especially those in middle-aged and elderly groups, show a marked increase in the incidence of CNS cancers, such as gliomas [12, 13]. This age-related rise in incidence is attributed to factors like cumulative environmental exposures, and genetic mutations [14]. Shifts in the demographic patterns of CNS cancer incidence suggest variation in exposure to environmental factors, and possibly lifestyle changes [15, 16].

The World Health Organization (WHO) categorizes CNS malignancies into distinct histological classes, confounding the traditional benign-malignant classification system in favor of a more comprehensive grading system [17, 18]. The epidemiology of CNS tumors, including their frequency, incidence, management, and recurrence rates, varies significantly based on histological type, age at diagnosis, and gender, and consequently, the available treatment modalities differ among these variables [17, 18]. Understanding these trends is crucial for tailoring clinical management strategies and guiding research efforts aimed at unraveling the complex etiology of CNS cancers [19, 20]. Recent studies have indicated a global increase in CNS tumor incidence, attributed partly to enhanced detection techniques [21, 22]. The advent of sophisticated diagnostic tools has led to improved identification of CNS tumors, including detection in asymptomatic individuals [23, 24].

Etiological Factors in CNS Tumour Development
Identifying risk factors is crucial for pinpointing populations at higher risk for CNS cancers and tailoring intervention strategies. The etiology of brain tumors remains elusive, although genetic mutations, developmental anomalies, and environmental factors are suspected contributors [25, 26].

High-throughput genomic studies have shed light on potential causative factors and risk elements associated with CNS tumors [27]. Research has identified several risk factors, including exposure to ionizing radiation and a history of

allergies, with the latter showing a stronger correlation in pediatric populations [28]. Studies suggested a link between European ancestry and an increased risk of childhood ependymoma [29] and a correlation between enlarged telomeres and heightened ependymoma risk in adolescents [30]. The relationship between higher birth weights and childhood CNS tumor incidence has been demonstrated by multiple meta-analyses [27, 30, 31], although some studies report conflicting findings [32]. Chromosomal structural anomalies are recognized as significant risk factors for pediatric cancers, particularly in children under five [33-37], with a twofold increased risk of CNS tumors in children with congenital disabilities [36-39].

The potential carcinogenic effects of ubiquitous mobile phone use have also been scrutinized. The International Agency for Research on Cancer (IARC) classified radiofrequency fields from cell phones as possibly carcinogenic in 2011 [40], although studies on extremely low-frequency magnetic fields (ELF-MF) have yielded inconclusive results [41]. A notable study linked high ELF-MF exposure to an increased risk of glioma [42].

Most CNS tumors are sporadic and only a small percentage of patients have a familial predisposition [43, 44]. In Saudi Arabia, CNS cancers are relatively rare compared to global statistics, with metastatic carcinoma and high-grade gliomas being the most prevalent [17]. Benign tumors were observed more frequently in females and malignant CNS tumors were higher in males than females, particularly those over 40 [7, 39]. A detailed understanding of CNS tumor prevalence in Saudi Arabia can illuminate disease variability across populations and uncover disparities in incidence and mortality rates.

The primary aim of this study is to conduct a comprehensive analysis of the epidemiological trends of Central Nervous System (CNS) cancers in Saudi Arabia, focusing on understanding the incidence and mortality rates. This analysis seeks to compare these rates with global statistics to identify unique regional trends and patterns specific to the Saudi Arabian context. Additionally, the study aims to explore the demographic variability in the incidence of CNS cancers within Saudi Arabia. It specifically investigates the age-specific incidence rates, highlighting the differences in the burden of CNS tumors across various age groups and focusing on comparing pediatric populations to adult demographics.

MATERIALS AND METHODS
Data Acquisition and Source Analysis
This study adopted a methodology from the Global Burden of Disease study [45], utilizing a comprehensive data collection and analysis approach. The primary data source was the Institute for Health Metrics and Evaluation (IHME) database, from which CNS cancer data from 1990 to 2019 were extracted. This dataset included detailed information on the

incidence, prevalence, and mortality rates of CNS cancers in Saudi Arabia, providing a robust foundation for our epidemiological analysis [46].

In addition to the IHME database, this study incorporated data from the Saudi Cancer Registry. This registry is a critical resource for cancer data in Saudi Arabia, offering valuable insights into the local epidemiological trends and patterns of CNS cancers [47]. Integrating data from the Saudi Cancer Registry was instrumental in ensuring a comprehensive understanding of the CNS cancer landscape within the Saudi Arabian context, allowing for a more nuanced and region-specific analysis [48].

Ethical Considerations in Data Utilization

Data from the Saudi Arabian National Cancer Database was utilized with approval from the Committee for Research Ethics for the Health of Makkah Region, Ministry of Health (H-02-K-076-0103-268).

Data Analysis and Visualisation

Data analysis in February 2023 involved descriptive statistics using Excel for gender and year-wise prevalence on GBD prevalence data. Excel was used to visualize CNS cancer's cause of death in Saudi Arabia and its age distribution pattern. SPSS (version 26) facilitated statistical comparisons and confidence intervals of 95% (95%CI).

RESULTS AND DISCUSSION

Escalating Incidence of CNS Cancers in Saudi Arabia over 30 years

From 1990 to 2019, Saudi Arabia recorded 75,667 CNS cancer cases, with males comprising 56.3%. The incidence rate escalated from 1.1 per 100,000 in 1990 to 3.63 per 100,000 in 2019 (**Figure 1**).
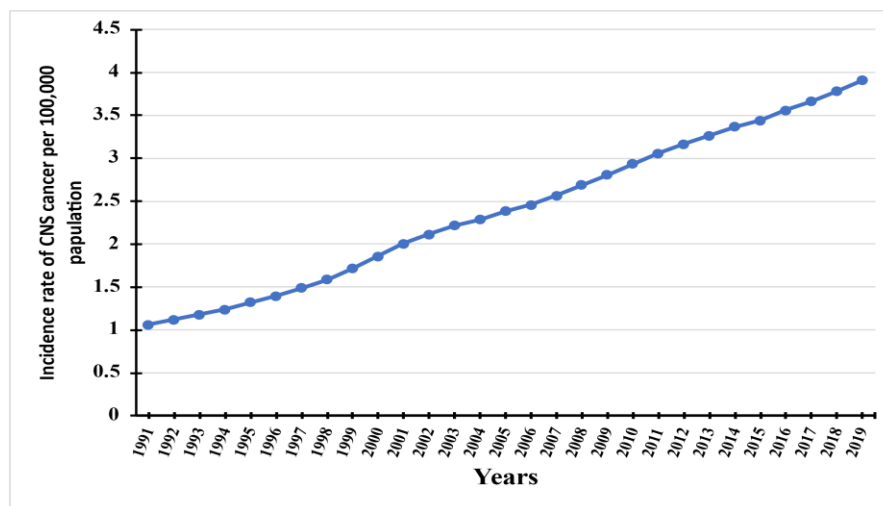
Figure 1. CNS cancer incidence in Saudi Arabia over 30 years. Figure presents a line graph depicting the incidence rates of CNS cancers in Saudi Arabia over 29 years, from 1990 to 2019. The X-axis of the graph represents the years, while the Y-axis indicates the incidence rates per 100,000 population.

The current study provides an extensive analysis of the epidemiology of CNS cancers in Saudi Arabia over a period spanning from 1990 to 2019. A key finding is the observed increase in the incidence of CNS cancers, coupled with a concurrent decline in mortality rates. Notably, while the incidence rate in Saudi Arabia is on an upward trajectory, it remains comparatively lower than those reported in more developed regions [29]. This difference may be attributed to genetic, environmental, and lifestyle factors and variations in healthcare systems and cancer screening programs.

This investigation into the epidemiological trends of CNS cancers in Saudi Arabia has revealed a notable increase in incidence rates, rising from 1.1 to 3.63 per 100,000 by 2019. This escalation mirrors trends observed in the broader Middle East and North African regions, where a similar upsurge in CNS cancer prevalence has been documented [46, 49].

However, the incidence rate in Saudi Arabia, peaking at 3.63 per 100,000, remains comparatively lower than that reported in developed countries such as Europe, Australia, and the USA, where incidence rates are higher [29]. Globally, age-standardized incidence rates have maintained a steady level of approximately 1.1% from 2010 to 2019 despite an overall increase in the total cancer burden.

Demographic Variability in CNS Cancer Incidence and Mortality

In examining the incidence rates of CNS cancers in Saudi Arabia over 30 years, our analysis revealed distinct age-related trends. The incidence rates remained consistently stable for the pediatric and adolescent age groups (0-14 and 15-19 years). In stark contrast, a significant increase was observed in the adult population, particularly in the 20-54 age group, where the incidence rate escalated ninefold by 2019

compared to 1990. Notably, the data indicated that individuals aged 55 and over have become increasingly susceptible to CNS cancers in the last two decades, marking them as the highest-risk group **(Figures 2a and 2b)**.

a)

b)
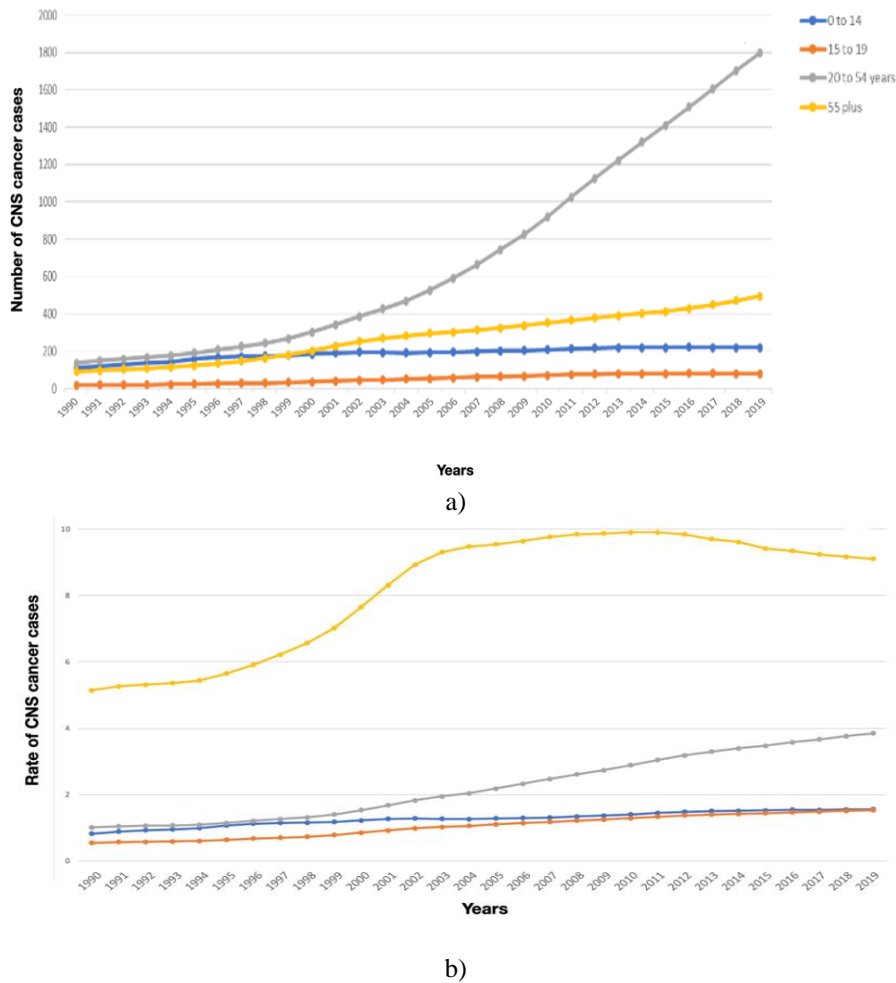
Figure 2. Age Group Analysis of CNS Cancer Incidence and Rate of Increase (1990-2019)
a) Incidence of CNS Cancer Cases by Age Group. This chart displays the number of CNS cancer cases across different age groups from 1990 to 2019. The X-axis represents the years from 1990 to 2019, while the Y-axis shows the incidence of cases. The lines illustrate the trends and fluctuations in the number of CNS cancer cases within each age group over 29 years. b) Rate of Increase in CNS Cancer Cases by Age Group. This chart focuses on the rate of increase in CNS cancer cases, again segmented by age group. The X-axis details the years from 1990 to 2019, and the Y-axis represents the rate of increase in cases. Each colored line traces the trajectory of the rate at which CNS cancer cases have increased within each age group, providing a comparative view of the acceleration or deceleration in case numbers across different age demographics. Four lines, each representing an age group, are color-coded for clarity: 0-14 (blue line), 15-19 (orange), 20-54 (grey), and 55+ (yellow).

The study highlights a significant increase in CNS cancer incidence in the age group of 55 and older, followed by the 20 to 54 age groups. This pattern agrees with findings from regional studies in Lebanon, the United Arab Emirates, and Jordan [47, 49-51], suggesting potential socio-geographical factors influencing these trends. The observed increase in CNS malignancies over time, particularly among the elderly, is a trend that has been documented globally [21, 22, 24, 48, 52-54]. Research indicates that the incidence of CNS cancers escalates with advancing age, especially in individuals aged 80 and above [12, 46].

Gender-Based Disparities in Incidence and Mortality
In the analysis of 75,667 CNS cancer cases in Saudi Arabia, a gender disparity was evident, with 42,593 cases in males and 33,074 in females. As depicted in **Figure 3a**, the data indicated that the 15-19 age group had the lowest incidence among all CNS patients. In contrast, the age group of 20-54 years exhibited the highest number of incidences. Notably, the incidence rate peaked in the 55 and over age group. This trend was more noticeable in males, who consistently showed higher incidence rates across all age groups, with the disparity

between genders widening significantly in the 55 and over category. Furthermore, **Figure 3b** illustrates that the 55+ age group also experienced the highest mortality rate,

underscoring the increased vulnerability of this demographic to CNS cancer-related fatalities.
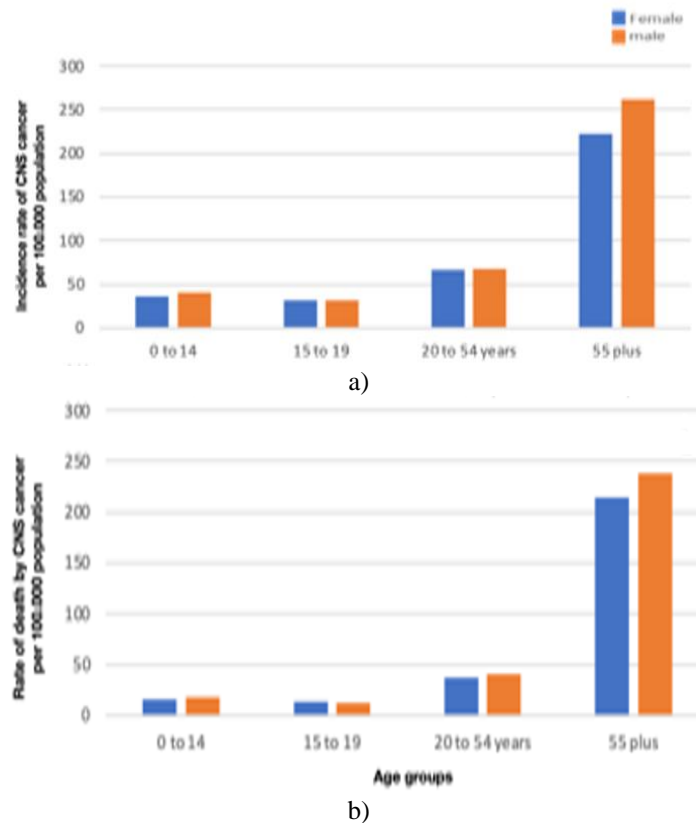
Figure 3. Age Group Analysis of CNS Cancer Incidence and Rate of Increase (1990-2019).
a) Incidence of CNS Cancer Cases by Age Group: This bar chart displays the number of CNS cancer cases across different age groups from 1990 to 2019, segregated by gender, male (orange) and Female (blue). The X-axis represents the years from 1990 to 2019, while the Y-axis shows the incidence of cases. The lines illustrate the trends and fluctuations in the number of CNS cancer cases within each age group over 29 years. b) Rate of Increase in CNS Cancer Cases by Age Group: This bar chart focuses on the rate of increase in CNS cancer cases, again segmented by age group segregated by gender, male (orange) and Female (blue). The X-axis details the years from 1990 to 2019, and the Y-axis represents the rate of increase in cases. Each bar traces the trajectory of the rate at which CNS cancer cases have increased within each age group, providing a comparative view of the acceleration or deceleration in case numbers across different age demographics.

Furthermore, the study highlights significant gender disparities in both incidence and mortality rates of CNS cancers in Saudi Arabia. Males consistently exhibited higher rates than females, which aligns with global epidemiological patterns [22, 24, 46, 55]. This gender-based variation in CNS cancer incidence and mortality could be influenced by a combination of biological, environmental, and lifestyle factors and warrants further investigation to understand the underlying causes.

This study's findings contribute to the global understanding of CNS cancer epidemiology, particularly regarding gender disparities and age-related prevalence. Consistent with existing literature [22, 46, 55, 56], our analysis indicates that male patients across all age groups exhibit a higher prevalence of CNS malignancies. This gender-based

prevalence aligns with research focused on neuroepithelial tumors in the Eastern Province of Saudi Arabia, which are more commonly observed in males and patients under the age of 49 [51, 57]. However, these tumors appear to be less prevalent in older age groups.

These findings underscore the complex interplay of age and gender in the epidemiology of CNS cancers. They also highlight the need for further research into these trends' underlying mechanisms, including potential hereditary and environmental factors. The comparative analysis of regional and international data provides valuable insights into the variations and similarities in CNS cancer incidence, contributing to a more nuanced understanding of its global epidemiology.

Mortality Trends: A Comparative Analysis

In assessing the mortality trends associated with CNS cancers in Saudi Arabia over a three-decade span, a line chart was utilized to depict the percentage of deaths relative to the total number of diagnosed cases. This analysis revealed a notable decrease in the mortality rate from 25% in 1990 to below 10%

by 2019. This decline became particularly pronounced post-2003. When disaggregated by gender, the data indicated a consistently higher mortality rate among males than females throughout the study period. However, the downward trajectory in mortality rates was observed to be parallel in both genders over the 30-year timeframe, as illustrated in **Figure 4**.
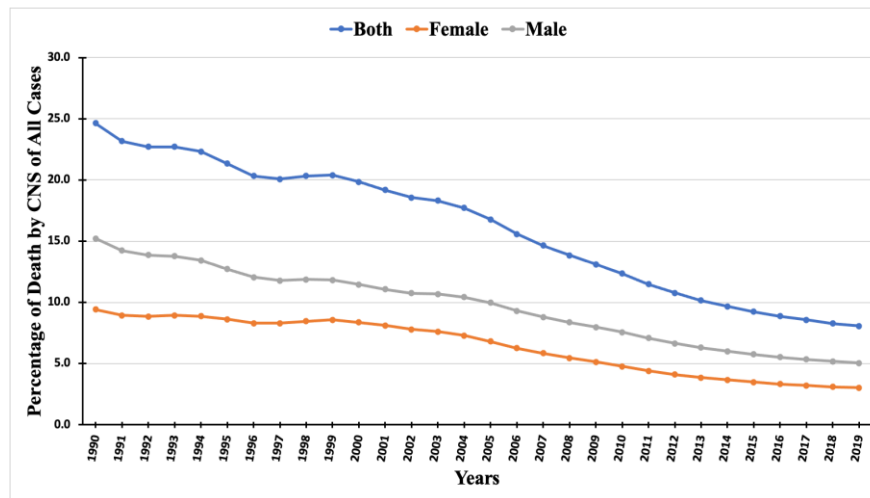
Figure 4. Trend in CNS Cancer Mortality Percentage per year in Saudi Arabia (1990-2019)
This line chart illustrates the reduction in deaths due to CNS cancers in Saudi Arabia over 30 years. This visualization effectively captures the overall declining trend in CNS cancer mortality rates in Saudi Arabia while also highlighting the gender-specific mortality trends within the same period. The X-axis of the chart is marked with years, ranging from 1990 to 2019. The Y-axis quantifies the annual percentage of deaths due to CNS cancers, calculated as a proportion of all diagnosed cases yearly. The chart employs three colored lines to represent different categories: (blue) males and females, (orange) females, and (grey) males.

A pivotal finding of this study is the discernible decline in the mortality rate associated with CNS tumors in Saudi Arabia, marking a significant shift in the trajectory of these cancers. This decline is likely due to advancements in diagnostic techniques, improvements in clinical practices, enhancements in cancer registration systems, and the evolution of therapeutic approaches. The impact of early detection, refined molecular diagnostics, and targeted interventions is evident in the reduced mortality rates observed globally for CNS tumors [58]. This aligns with the findings from the Global Burden of Disease (GBD) study, which indicated a decrease in the death-to-incidence ratio in regions with improvements in the Socio-Demographic Index (SDI) [58-60]. Furthermore, data from the National Cancer Institute corroborate this trend, showing an increase in the 5-year survival rate for CNS cancers from 26.8% in 1990 to 36.1% in 2009 [47]. In Saudi Arabia, this positive trend is reflected in the reduction of the mortality rate from 25% in 1990 to 10% by 2019, underscoring significant progress in managing CNS cancers.

Concurrently, the CONCORD-3 study has provided insights into the survival rates from CNS cancers, indicating a stabilization over 15 years. Notably, survival rate improvement from 3 to 10% was observed in countries with

a higher Socio-Demographic Index (SDI), predominantly high-income nations [61]. This improvement in survival rates can be attributed to the enhanced effectiveness of treatment modalities and the disparity in healthcare services across different demographic populations [56, 59, 61]. These findings suggest that advancements in medical treatments and healthcare infrastructure, more prevalent in higher SDI countries, are crucial in improving patient outcomes in CNS cancers.
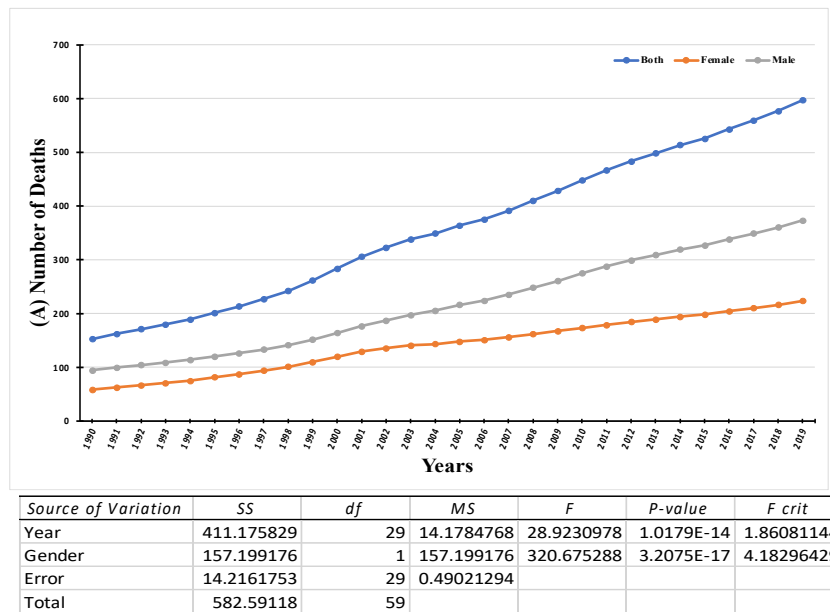
Contrasting Mortality Rates with Incidence Trends

Over the period from 1990 to 2019, there was a significant escalation in CNS cancer mortality in Saudi Arabia. **Figure 5a** graphically represents this trend, showing an overall increase in the percentage of patients death due to neurological cancers. Notably, the mortality rate among male patients was consistently higher than that observed in female patients. This gender-specific mortality trend is quantitatively depicted in **Figure 5b**, which illustrates the fold change in the number of deaths due to CNS cancer. The data reveal a mortality rate in 2019 that is nearly quadruple that of 1990.
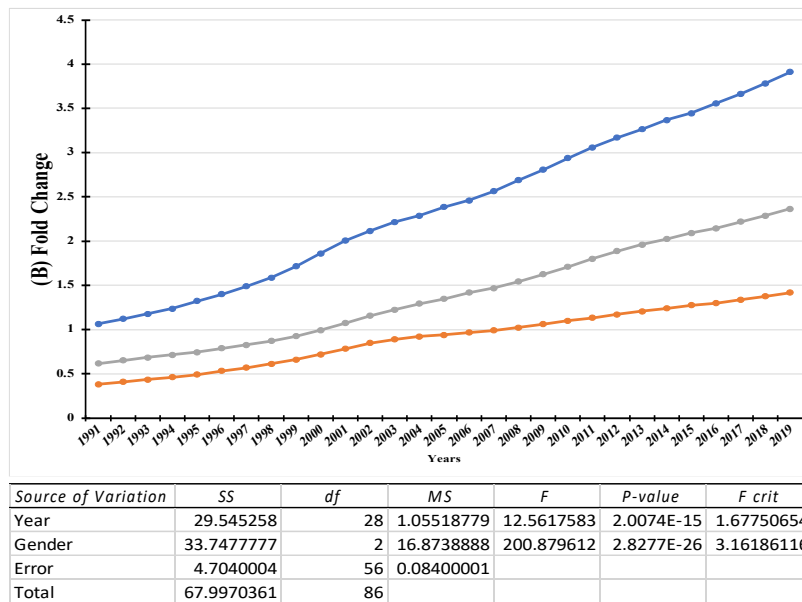
In **Figure 5**, three lines represent different categories of mortality data: a blue line indicates the total number of deaths each year, an orange line represents the annual number of

female deaths, and a grey line shows the total number of male deaths annually. This visual representation underscores the increasing trend in CNS cancer-related deaths over the 30 years, with a marked disparity between male and female mortality rates. Additionally, an ANOVA analysis was conducted to assess the statistical significance of these trends. The analysis confirmed that the variations in mortality rates over the 30 years and the differences between male and female mortality rates were statistically significant.

Source of Variation	SS	df	MS	F	P-value	F crit
Year	411.175829	29	14.1784768	28.9230978	1.0179E-14	1.86081144
Gender	157.199176	1	157.199176	320.675288	3.2075E-17	4.18296429
Error	14.2161753	29	0.49021294			
Total	582.59118	59				

a)

Source of Variation	SS	df	MS	F	P-value	F crit
Year	29.545258	28	1.05518779	12.5617583	2.0074E-15	1.67750654
Gender	33.7477777	2	16.8738888	200.879612	2.8277E-26	3.16186116
Error	4.7040004	56	0.08400001			
Total	67.9970361	86				

b)

Figure 5. Trends in CNS Cancer Mortality in Saudi Arabia by Gender (1990-2019)
Figure 5 presents a series of line charts illustrating the trends in mortality due to CNS cancers in Saudi Arabia over 30 years, differentiated by gender. a) line chart of the number of deaths from 1990-2019 by gender. b) lone chart of the fold change of death annually from 1990-2019. The charts are composed of three distinct lines, each representing a different aspect of the mortality data: (blue) both male and female patients, (orange) female), and (grey) male. Additionally, the figure includes the results of an ANOVA analysis, which confirms the statistical significance of the observed trends in CNS cancer mortality, both over time and between genders. This analysis underscores the importance of the findings in understanding the evolving landscape of CNS cancer mortality in Saudi Arabia.

Global Epidemiological Comparisons and Implications

The comparative analysis of CNS cancer trends in Saudi Arabia with international studies offers a broader perspective on the global epidemiology of these malignancies. The increasing trend of CNS cancers observed in Saudi Arabia reflects a broader global pattern. Studies from various regions, including North America, Europe, and Asia, have reported similar increases in CNS cancer incidence, suggesting a global rise in these malignancies [24]. This trend may be attributed to aging populations, environmental influences, and improved diagnostic capabilities [14, 62].

Interpreting CNS Cancer Trends in Saudi Arabia

In interpreting the CNS cancer trends in Saudi Arabia, it is crucial to consider the region's unique socio-demographic and healthcare context. The study's findings, which indicate a lower incidence rate in Saudi Arabia than in developed countries, might be influenced by regional differences in genetic predispositions, lifestyle factors, and healthcare access [63]. Additionally, the advancements in healthcare infrastructure and cancer care in Saudi Arabia could contribute to the observed decline in mortality rates, mirroring global trends toward improved cancer management [64].

Global Epidemiological Comparisons and Implications

The broader implications of this study extend beyond the regional context, contributing to the global understanding of CNS cancer epidemiology. The gender disparities and age-related prevalence patterns observed in Saudi Arabia align with global data, underscoring the need for gender-specific and age-targeted approaches in CNS cancer research and treatment [24, 64]. Furthermore, the study highlights the importance of international collaboration in cancer research, as understanding the variations in cancer trends across different regions can lead to more effective global cancer control strategies [65].

CONCLUSION
Summary of Key Findings and Implications

This comprehensive study has provided valuable insights into the epidemiological trends of CNS cancers in Saudi Arabia over 30 years, from 1990 to 2019. The key findings reveal a notable increase in the incidence of CNS cancers, with the rates rising from 1.1 to 3.63 per 100,000 population. Despite this increase, the incidence rates in Saudi Arabia remain lower than those observed in more developed regions, suggesting regional variations in risk factors and healthcare practices.

A significant decline in mortality rates was also observed, decreasing from 25% in 1990 to below 10% in 2019. This decline indicates advancements in healthcare, particularly in early detection, molecular diagnostics, and therapeutic interventions. The study also highlighted gender disparities, with males exhibiting higher incidence and mortality rates, a trend consistent with global data.

The findings underscore the importance of continuous surveillance and research into CNS cancers. They highlight the need for targeted strategies to address the rising incidence and further reduce mortality rates. The gender disparities observed call for gender-specific research and healthcare approaches.

Future research should focus on understanding the underlying causes of the observed trends, including genetic, environmental, and lifestyle factors. International collaboration in research could provide a more comprehensive understanding of global variations in CNS cancer trends. Additionally, there is a need to explore new diagnostic and therapeutic technologies to improve patient outcomes further.

In conclusion, this study contributes significantly to understanding CNS cancer trends in Saudi Arabia, offering a foundation for future research and healthcare policy development aimed at combating these malignancies more effectively.

Prospects for Future Research and Policy Development

The findings of this study pave the way for future research endeavors and have substantial implications for health policy and cancer management strategies. There is an urgent need for comprehensive etiological studies that delve into the genetic, environmental, and lifestyle factors specific to the Saudi population, which could elucidate the underlying causes of CNS cancers. Additionally, the observed gender disparities in CNS cancer incidence and mortality rates necessitate gender-specific research to understand the contributing biological and socio-environmental factors, potentially leading to more personalized prevention and treatment approaches. Exploring novel diagnostic methods, such as advanced imaging techniques and liquid biopsies, alongside new treatment modalities like targeted therapies and immunotherapies could significantly enhance early detection and improve patient outcomes. Furthermore, international collaborative studies could provide valuable comparative data, helping to place the findings within a global context.

Regarding health policy and cancer management, these findings could inform the development of targeted screening programs and preventive strategies tailored to the specific high-risk factors in the Saudi population. Insights from this research could guide healthcare policy in strengthening the infrastructure for cancer care, including establishing specialized centers for CNS cancer treatment and research. Public health campaigns, informed by the data on increasing incidence rates and gender disparities, could raise awareness about CNS cancers, promote early detection, and encourage healthy lifestyle choices. Additionally, these findings could

influence policy formulation, particularly in resource allocation for cancer research, improving healthcare access, and developing national guidelines for CNS cancer management. Overall, this study sets a foundation for future initiatives to reduce the burden of CNS malignancies, focusing on improving outcomes through informed research and policymaking.

Advancing CNS Cancer Research: Genomic and Molecular Perspectives

Exploring genomic and molecular research holds immense potential in advancing our understanding and treatment of CNS cancers. Integrating genomic data into CNS cancer research can provide deeper insights into the molecular mechanisms underlying tumor development and progression. This approach could lead to the identification of novel biomarkers for early detection and prognosis and the discovery of new therapeutic targets. Personalized medicine, driven by genomic profiling, could revolutionize the treatment of CNS cancers by enabling more precise and effective interventions based on individual genetic makeup.

Moreover, molecular research can facilitate the understanding of drug resistance mechanisms in CNS cancers, paving the way for developing more effective treatment strategies. Studying epigenetic changes and the tumor microenvironment could also provide critical information about tumor behavior and response to therapy. Additionally, advancements in molecular imaging could enhance the visualization of tumor characteristics, aiding in more accurate diagnosis and treatment planning.

In the future, combining genomic and molecular research with emerging technologies such as artificial intelligence and machine learning could lead to ground-breaking developments in CNS cancer diagnosis and treatment. These technologies can potentially analyze complex genomic data more efficiently, predict treatment responses, and personalize patient care.

In conclusion, genomic and molecular research represents a frontier in CNS cancer research, offering promising avenues for improving patient outcomes. Continued investment in this field and interdisciplinary collaboration are essential for harnessing its full potential in the fight against CNS cancers.

While this study provides valuable insights into the epidemiological trends of CNS cancers in Saudi Arabia, it is essential to acknowledge certain limitations that may impact the interpretation and generalizability of the findings. Firstly, while comprehensive, the reliance on retrospective data from the Saudi Cancer Registry and the IHME database may be subject to inherent biases such as underreporting or misclassification of cases. This could potentially affect the accuracy of the incidence and mortality rates reported. Additionally, the study's retrospective nature limits our ability to establish causality between observed trends and

potential risk factors.

Another limitation is the lack of detailed patient-level data, which restricts our ability to analyze the impact of individual factors such as lifestyle, genetic predisposition, and environmental exposures on the incidence and progression of CNS cancers. Furthermore, while the study provides a comparative analysis of global trends, the specific socio-cultural and environmental context of Saudi Arabia might limit the applicability of these findings to other regions. The study also does not account for advancements in treatment modalities over the 30-year period, which could have influenced survival rates and mortality data. Recognizing these limitations is crucial for interpreting the study's findings and guiding future research directions.

REFERENCES

1. Galea-Holhoş LB, Delcea C, Siserman CV, Ciocan V. Age estimation of human remains using the dental system: A review. Ann Dent Spec. 2023;11(3):15.
2. Siserman C, Delcea C, Matei HV, Vică ML. Major affective distress in testing forensic paternity. Rom J Leg Med. 2019;27(3):292-6.
3. Miller KD, Ostrom QT, Kruchko C, Patil N, Tihan T, Cioffi G, et al. Brain and other central nervous system tumor statistics, 2021. CA Cancer J Clin. 2021;71(5):381-406.
4. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA: A Cancer J Clin. 2021;71(1):7-33.
5. Moin A, Rizvi SMD, Hussain T, Gowda DV, Subaiea GM, Elsayed MMA, et al. Current status of brain tumor in the Kingdom of Saudi Arabia and application of nanobiotechnology for its treatment: A comprehensive review. Life (Basel). 2021;11(5):421.
6. Mohammed AA, Hamdan AN, Homoud AS. Histopathological profile of brain tumors: A 12-year retrospective study from Madinah, Saudi Arabia. Asian J Neurosurg. 2019;14(4):1106-11.
7. Ostrom QT, Patil N, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS. Corrigendum to: CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the united states in 2013-2017. Neuro Oncol. 2022;24(7):1214.
8. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86.
9. Nicoară ND, Marian P, Petriş AO, Delcea C, Manole F. A review of the role of cognitive-behavioral therapy on anxiety disorders of children and adolescents. Pharmacophore. 2023;14(4):35-9.
10. Gherman C, Enache A, Delcea C. The multi-factorial determinism of forensic expertise regarding sentence interruption on medical grounds and decision. J Forensic Leg Med. 2019;61:45-55.

11. Hossain MJ, Xiao W, Tayeb M, Khan S. Epidemiology and prognostic factors of pediatric brain tumor survival in the US: Evidence from four decades of population data. Cancer Epidemiol. 2021;72:101942.

12. Arora RS, Alston RD, Eden TO, Estlin EJ, Moran A, Birch JM. Age-incidence patterns of primary CNS tumors in children, adolescents, and adults in England. Neuro Oncol. 2009;11(4):403-13.

13. Chen B, Chen C, Zhang Y, Xu J. Recent incidence trend of elderly patients with glioblastoma in the United States, 2000-2017. BMC Cancer. 2021;21(1):54.

14. Vienne-Jumeau A, Tafani C, Ricard D. Environmental risk factors of primary brain tumors: A review. Rev Neurol (Paris). 2019;175(10):664-78.

15. Rus M, Matei R, Sandu ML, Delcea C, Siserman C. Emotional distress and coping strategies of health care workers during COVID-19 pandemic. Rom J Leg Med. 2020;28:442-50.

16. Delcea C, Siserman C. Validation and standardization of the questionnaire for evaluation of paraphilic disorders. Rom J Leg Med. 2020;28(1):14-20.

17. Kurdi M, Butt NS, Baeesa S, Alghamdi B, Maghrabi Y, Bardeesi A, et al. Epidemiological distribution of primary central nervous system tumors in the western province of Saudi Arabia: A local registry from neuroscience-affiliated centers. Epidemiol Health. 2021;43:e2021037.

18. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO classification of tumors of the central nervous system: A summary. Neuro Oncol. 2021;23(8):1231-51.

19. Papageorgiou GI, Razis ED. CNS tumors in adolescents and young adults: The need for a holistic specialized approach. JCO Oncol Pract. 2020;16(4):155-62.

20. Radu CC, Delcea C, Plesa A, Rad D. Transforming perceptions of drug consumption among youth through a cognitive-social-medico-legal educational approach. Pharmacophore. 2023;14(4):50-6.

21. Ostrom QT, Francis SS, Barnholtz-Sloan JS. Epidemiology of brain and other CNS tumors. Curr Neurol Neurosci Rep. 2021;21(12):68.

22. Pineros M, Sierra MS, Izarzugaza MI, Forman D. Descriptive epidemiology of brain and central nervous system cancers in Central and South America. Cancer Epidemiol. 2016;44 Suppl 1:S141-S9.

23. Law M. Advanced imaging techniques in brain tumors. Cancer Imaging. 2009;9 Spec No A(Special issue A):S4-9.

24. Miranda-Filho A, Piñeros M, Soerjomataram I, Deltour I, Bray F. Cancers of the brain and CNS: Global patterns and trends in incidence. Neuro Oncol. 2017;19(2):270-80.

25. Poon MTC, Brennan PM, Jin K, Sudlow CLM, Figueroa JD. Might changes in diagnostic practice explain increasing incidence of brain and central nervous system tumors? A population-based study in Wales (United Kingdom) and the United States. Neuro Oncol. 2021;23(6):979-89.

26. Rigau V, Zouaoui S, Mathieu-Daudé H, Darlix A, Maran A, Trétarre B, et al. French brain tumor database: 5-year histological results on 25 756 cases. Brain Pathol. 2011;21(6):633-44.

27. Georgakis MK, Kalogirou EI, Liaskas A, Karalexi MA, Papathoma P, Ladopoulou K, et al. Anthropometrics at birth and risk of a primary central nervous system tumor: A systematic review and meta-analysis. Eur J Cancer. 2017;75:117-31.

28. Ostrom QT, Adel Fahmideh M, Cote DJ, Muskens IS, Schraw JM, Scheurer ME, et al. Risk factors for childhood and adult primary brain tumors. Neuro Oncol. 2019;21(11):1357-75.

29. Zhang C, Ostrom QT, Hansen HM, Gonzalez-Maya J, Hu D, Ziv E, et al. European genetic ancestry associated with risk of childhood ependymoma. Neuro Oncol. 2020;22(11):1637-46.

30. Zhang C, Ostrom QT, Semmes EC, Ramaswamy V, Hansen HM, Morimoto L, et al. Genetic predisposition to longer telomere length and risk of childhood, adolescent, and adult-onset ependymoma. Acta Neuropathol Commun. 2020;8(1):173.

31. Dahlhaus A, Prengel P, Spector L, Pieper D. Birth weight and subsequent risk of childhood primary brain tumors: An updated meta-analysis. Pediatr Blood Cancer. 2017;64(5):e26299.

32. Bailey HD, Rios P, Lacour B, Guerrini-Rousseau L, Bertozzi AI, Leblond P, et al. Factors related to pregnancy and birth and the risk of childhood brain tumors: The ESTELLE and ESCALE studies (SFCE, France). Int J Cancer. 2017;140(8):1757-69.

33. Johnson KJ, Lee JM, Ahsan K, Padda H, Feng Q, Partap S, et al. Pediatric cancer risk in association with birth defects: A systematic review. PLoS One. 2017;12(7):e0181246.

34. Lupo PJ, Schraw JM, Desrosiers TA, Nembhard WN, Langlois PH, Canfield MA, et al. Association between birth defects and cancer risk among children and adolescents in a population-based assessment of 10 million live births. JAMA Oncol. 2019;5(8):1150-8.

35. Mili F, Lynch CF, Khoury MJ, Flanders WD, Edmonds LD. Risk of childhood cancer for infants with birth defects. II. A record-linkage study, Iowa, 1983-1989. Am J Epidemiol. 1993;137(6):639-44.

36. Botto LD, Flood T, Little J, Fluchel MN, Krikov S, Feldkamp ML, et al. Cancer risk in children and adolescents with birth defects: A population-based cohort study. PLoS One. 2013;8(7):e69077.

37. Janitz AE, Neas BR, Campbell JE, Pate AE, Stoner JA, Magzamen SL, et al. Childhood cancer in children with congenital anomalies in Oklahoma, 1997 to 2009. Birth Defects Res A Clin Mol Teratol. 2016;106(7):633-42.

38. Bjørge T, Cnattingius S, Lie RT, Tretli S, Engeland A. Cancer risk in children with birth defects and their families: a population-based cohort study of 5.2 million children from Norway and Sweden. Cancer Epidemiol Biomarkers Prev. 2008;17(3):500-6.

39. Fisher PG, Reynolds P, Von Behren J, Carmichael SL, Rasmussen SA, Shaw GM. Cancer in children with nonchromosomal birth defects. J Pediatr. 2012;160(6):978-83.

40. Baan R, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, et al. Carcinogenicity of radiofrequency electromagnetic fields. Lancet Oncol. 2011;12(7):624-6.

41. Turner MC, Benke G, Bowman JD, Figuerola J, Fleming S, Hours M, et al. Occupational exposure to extremely low-frequency magnetic fields and brain tumor risks in the INTEROCC study. Cancer Epidemiol Biomarkers Prev. 2014;23(9):1863-72.

42. Carles C, Esquirol Y, Turuban M, Piel C, Migault L, Pouchieu C, et al. Residential proximity to power lines and risk of brain tumor in the general population. Environ Res. 2020;185:109473.

43. Wrensch M, Lee M, Miike R, Newman B, Barger G, Davis R, et al. Familial and personal medical history of cancer and nervous system conditions among adults with glioma and controls. Am J Epidemiol. 1997;145(7):581-93.

44. Melin BS, Barnholtz-Sloan JS, Wrensch MR, Johansen C, Il'yasova D, Kinnersley B, et al. Genome-wide association study of glioma subtypes identifies specific differences in genetic susceptibility to glioblastoma and non-glioblastoma tumors. Nat Genet. 2017;49(5):789-94.

45. Mortality GBD, Causes of Death C. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the global burden of disease study 2013. Lancet. 2015;385(9963):117-71.

46. Saeidi Borojeni HR, Najafi F, Khosravi Shadmani F, Darabi Z, Darbandi M, Farhadi K, et al. Disability-adjusted life years and mortality rate attributed to brain and central nervous system cancer in the middle east and north Africa countries. Neuroepidemiology. 2021;55(6):447-59.

47. Khan S, Kambris MEK, AlShamsi ET. Epidemiology of brain tumors in the United Arab Emirates: A national registry cross-sectional study. BMC Neurol. 2020;20(1):301.

48. Salimi A, Zali A, Seddighi AS, Seddighi A, Meshkat S, Hosseini M, et al. Descriptive epidemiology of brain and central nervous system tumours: Results from Iran national cancer registry, 2010-2014. J Cancer Epidemiol. 2020;2020:3534641.

49. Tamimi AF, Tamimi I, Abdelaziz M, Saleh Q, Obeidat F, Al-Husseini M, et al. Epidemiology of malignant and non-malignant primary brain tumors in Jordan. Neuroepidemiology. 2015;45(2):100-8.

50. El Hage S, Kawtharani M, Nabha S, El Masri J, Saad M. Distribution of primary brain tumor subtypes in Lebanon: A multicenter eleven-year study of 695 patients. Cureus. 2021;13(9):e17918.

51. Almatroudi A. Brain tumors in Saudi Arabia: An observational and descriptive epidemiological analysis. Healthcare (Basel). 2022;10(9):1796.

52. He Z, Wong ST, Yam KY. Newly-diagnosed, histologically-confirmed central nervous system tumours in a regional hospital in Hong Kong: An epidemiological study of 21 years. J Korean Neurosurg Soc. 2020;63(1):119-35.

53. Pouchieu C, Gruber A, Berteaud E, Menegon P, Monteil P, Huchet A, et al. Increasing incidence of central nervous system (CNS) tumors (2000-2012): Findings from a population-based registry in Gironde (France). BMC Cancer. 2018;18(1):653.

54. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.

55. Nomura E, Ioka A, Tsukuma H. Trends in the incidence of primary intracranial tumors in Osaka, Japan. Jpn J Clin Oncol. 2011;41(2):291-4.

56. Mortazavi SMJ, Mortazavi SAR, Paknahad M. Cancers of the brain and CNS: Global Patterns and trends in incidence. J Biomed Phys Eng. 2018;8(1):151-2.

57. Taha MS, Almsned FM, Hassen MA, Atean IM, Alwbari AM, Alharbi QK, et al. Demographic and histopathological patterns of neuro-epithelial brain tumors in Eastern Province of Saudi Arabia. Neurosciences (Riyadh). 2018;23(1):18-22.

58. Global Burden of Disease Cancer C, Kocarnik JM, Compton K, Dean FE, Fu W, Gaw BL, et al. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: A systematic analysis for the global burden of disease study 2019. JAMA Oncol. 2022;8(3):420-44.

59. Coleman MP. Cancer survival: Global surveillance will stimulate health policy and improve equity. Lancet. 2014;383(9916):564-73.

60. Mohammadi E, Ghasemi E, Azadnajafabad S, Rezaei N, Saeedi Moghaddam S, Ebrahimi Meimand S, et al. A global, regional, and national survey on burden and quality of Care Index (QCI) of brain and other central nervous system cancers; global burden of disease systematic analysis 1990-2017. PLoS One. 2021;16(2):e0247120.

61. Allemani C, Coleman MP. Public health surveillance of cancer survival in the United States and worldwide: The contribution of the CONCORD programme. Cancer. 2017;123 Suppl 24(Suppl 24):4977-81.

62. Pulumati A, Pulumati A, Dwarakanath BS, Verma A, Papineni RVL. Technological advancements in cancer diagnostics: Improvements and limitations. Cancer Rep (Hoboken). 2023;6(2):e1764.

63. Salhab HA, Khachfe HH, Fares MY, Belkacemi Y, Hosseini H. Central nervous system cancers in the Middle East and North Africa (MENA) region: where does Lebanon stand. Chin Clin Oncol. 2020;9(3):36.

64. Fan Y, Zhang X, Gao C, Jiang S, Wu H, Liu Z, et al. Burden and trends of brain and central nervous system cancer from 1990 to 2019 at the global, regional, and country levels. Arch Public Health. 2022;80(1):209.

65. Trimble EL, Abrams JS, Meyer RM, Calvo F, Cazap E, Deye J, et al. Improving cancer outcomes through international collaboration in academic cancer treatment trials. J Clin Oncol. 2009;27(30):5109-14.