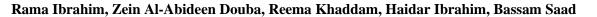


Clinical and Demographic Profile of Syrian Patients with Malignant Glioma: A Six-Month Retrospective Analysis



Abstract: This study presents a retrospective analysis of glioblastoma cases admitted to Tishreen University Hospital in Lattakia, Syria, between February and August 2024. The study examines the several potential risk factors including age, sex, genetic predispositions, and lifestyle factors such as smoking and alcohol consumption. It also explores the most commonly encountered tumor grade and the presence of various neurological symptoms, as well as treatment outcomes. A total of 30 glioblastoma were enrolled in this study, 63% of which were males, and the highest age incidence was between 40 and 50 years. Only 6% had a family history of glioblastoma, and 66% of the patients were smokers. Memory disorders, visual impairments, and headaches were common symptoms, with 100% of the patients reporting nausea and vomiting. Glioblastoma diagnosis was primarily established through MRI with contrast (76%), and the predominant treatment modality was surgery combined with radiotherapy and chemotherapy (80%). Posttreatment relapse occurred in 26% of the patients, with a median remission period of four months. These findings provide important insights into the clinical characteristics and treatment outcomes of glioblastoma patients in this region.

Keywords: Glioblastoma, Clinical Characteristics, Neurological Symptoms, Risk factors, Treatment Outcomes

I. INTRODUCTION

Glioblastoma (GBM) is the most common and aggressive form of primary brain tumor in adults, posing a major challenge in neuro-oncology due to its highly invasive nature and rapid progression [1].

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* Correspondence Author (s)

Dr. Rama Ibrahim*, Department of Biochemistry and Microbiology, Faculty of Pharmacy, Al-Sham Private University (ASPU), Lattakia, Syria. E-mail: <u>r.i.foph.lat@aspu.edu.sy</u>, ORCID ID: <u>0009-0007-1516-6870</u>

Zein Al-Abideen Douba, Department of Biochemistry and Microbiology, Faculty of Pharmacy, Tishreen University, Lattakia, Syria. E-mail: <u>zeinalaabdin.douba@gmail.com</u>, ORCID ID: <u>0009-0007-5524-</u> 8408

Reema Khaddam, Department of Biochemistry and Microbiology, Faculty of Pharmacy, Al-Sham Private University (ASPU), Lattakia, Syria. E-mail: <u>reemakhaddam@gmail.com</u>

Haidar Ibrahim, Department of Biochemistry and Microbiology, Faculty of Pharmacy, Al-Sham Private University (ASPU), Lattakia, Syria. E-mail: haidaribrahem484@gmail.com

Dr. Bassam Saad, Department of Oncology, Faculty of Medicine, Tishreen University, Lattakia, Syria. E-mail: <u>bassamf@gmail.com</u>

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This tumor is characterized by significant heterogeneity, meaning that it consists of a diverse mix of cell types and genetic profiles, contributing to its resistance conventional therapies [2]. GBM is notorious for its poor prognosis, with standard treatments such as surgery, radiation therapy, and chemotherapy often providing only limited efficacy [2]. Despite extensive research and advancements in therapeutic strategies, the median survival time for patients diagnosed with GBM remains tragically low, typically between 12 to 15 months post-diagnosis [3].One of the key reasons behind the poor outcomes associated with GBM is its ability to invade surrounding brain tissues, making complete surgical resection nearly impossible [4]. Even with aggressive treatment, the tumor often recurs, contributing to the dismal survival rates [4]. Additionally, GBM has a complex microenvironment that supports tumor growth and shields it from the immune system, further complicating treatment efforts [5]. This multifactorial resistance has driven ongoing research into therapies, including targeted novel treatments, immunotherapy, and personalized medicine, although these approaches have yet to significantly improve survival rates [5].

A. Global Epidemiology of Glioblastoma

The incidence of glioblastoma is relatively low compared to other cancers, with an estimated rate of 3.2 cases per 100,000 people worldwide [6]. However, its aggressive nature and high mortality rate make it a critical focus of research [6]. The disease primarily affects older adults, with the average age of diagnosis being around 64 years [7]. Men are slightly more likely to be diagnosed with GBM than women [7].

Globally, the burden of glioblastoma is further exacerbated by disparities in healthcare access and resources [8]. In high-income countries, advanced diagnostic tools like MRI and CT scans, along with state-of-the-art treatment options, are readily available [8]. However, in low- and middle-income countries, including those in the Middle East and Africa, limited access to these essential healthcare services often leads to delayed diagnosis and suboptimal treatment [9]. This disparity results in significantly worse outcomes for patients in resource-limited settings [9].

In Syria, the challenges faced by patients with glioblastoma are compounded by the ongoing conflict and the resulting strain on the healthcare system [10].

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Comprehensive national statistics on glioblastoma incidence and prevalence are scarce since healthcare infrastructure in many areas has been severely impacted, leading to difficulties in diagnosis, treatment, and follow-up care [10]. Hospitals and medical facilities may lack the advanced imaging equipment and specialized surgical expertise required for optimal GBM management [10].

Moreover, the socio-economic hardships faced by many Syrians further limit access to healthcare [11]. The cost of treatments like chemotherapy and radiotherapy, which are essential for managing glioblastoma, can be prohibitive for many patients [11]. Additionally, the availability of neurosurgeons and oncology specialists is limited, which may further compromise patient outcomes [12]. As a result, the prognosis for glioblastoma patients in Syria is likely even worse than the already poor global average [12].

II. STUDY OVERVIEW

This study, conducted at Tishreen University Hospital in Latakia-Syria, seeks to provide a detailed analysis of glioblastoma cases diagnosed at the institution. We will examine key clinical factors such as the age of onset, tumor grade and type, and initial presenting symptoms. In addition, demographic data such as gender distribution, will be assessed to better understand patterns that may influence disease progression and outcomes in the Syrian context. By evaluating the treatment regimens offered to patients, including the rates of surgical resection, responses to radiotherapy and chemotherapy, and overall survival rates, this study aims to identify specific gaps in care.

Through this investigation, we aim to shed light on the particular challenges faced by glioblastoma patients in Syria and other resource-limited settings. This study may provide insights that help shape future clinical guidelines and foster global efforts on international initiatives that could help improving patient outcomes and address unique challenges in regions with similar limited healthcare infrastructure, both regionally and globally.

III. MATERIALS AND METHODS

This descriptive study involved the collection of data from 30 glioblastoma patients treated at Tishreen University Hospital over a six-month period, from February to August 2024. The aim of this study was to gather a detailed account of the clinical characteristics and treatment experiences of these patients. Patient information was meticulously extracted from hospital records, encompassing a wide range of variables that provide insights into the patient population. These variables included demographic data such as age and sex, family history of cancer, lifestyle habits (including smoking and alcohol consumption), presenting symptoms, tumor type and grade, diagnostic methods, and treatment protocols.

The primary objective was to describe the characteristics of glioblastoma cases in our region and identify any notable trends or patterns related to patient outcomes, particularly focusing on survival rates and relapse occurrences. By examining these factors, the study aimed to enhance understanding of glioblastoma in this specific cohort.

Ethical considerations were paramount throughout the study. It adhered to the ethical standards set by the hospital's review board, ensuring that all patient data were collected and handled in a manner that respects patient privacy. All data were anonymized to ensure confidentiality and to protect the identities of the individuals involved.

IV. RESULTS

A. Age Distribution

The patient cohort was diverse in terms of age. The breakdown was as follows: 6% of patients were between 10-20 years old, 16% were between 20-30 years old, 13% were between 30-40 years old, 23% fell within the 40-50 age range, and 13% each in the 50-60, 60-70, and 70-80 age brackets. This distribution indicates that while glioblastoma is more common in older adults, a significant portion of patients in this study were younger, under the age of 50.

B. Gender Distribution

Out of the total cohort, 63% were males, and 37% were females, reflecting the known male predominance in glioblastoma cases. This aligns with global epidemiological data, which consistently show that men are at a higher risk of developing glioblastoma compared to women (Figure 1).

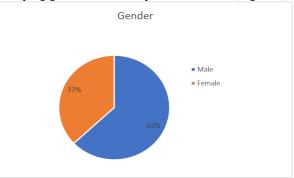


Figure 1: Gender Distribution of Glioblastoma Patients (63% Male, 37% Female)

C. Tumor Differentiation

The majority of patients (60%) had low-grade glioblastoma at the time of diagnosis, while the remaining 40% had high-grade tumors. High-grade tumors are known to have a more aggressive course and worse prognosis, which is consistent with global trends in glioblastoma progression (Figure 2).

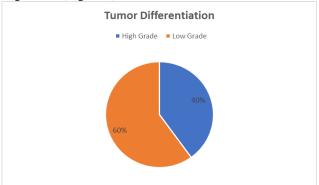


Figure 2: Distribution of Patients According to the Degree of Disease Differentiation

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D. Smoking and Alcohol Consumption

Lifestyle habits were notable in this cohort, with 66% of patients identified as smokers and 46% reporting alcohol consumption. These habits have been implicated in various forms of cancer, and while their direct role in glioblastoma is not fully established, they may contribute to overall health deterioration and complicate treatment (Figures 3,4).

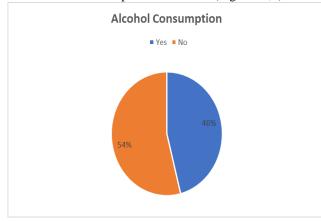


Figure 2 :Distribution of Patients According to Alcohol Consumption

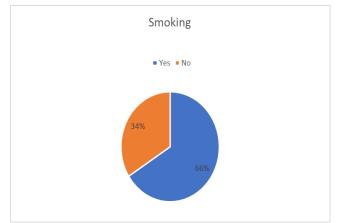
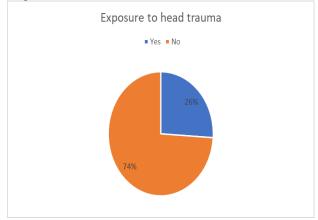
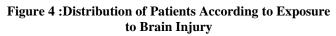


Figure 3: Distribution of Patients According to Smoking

E. Brain Injuries Potentially Related to Glioblastoma Development

After interrogation, 26% of patients reported a history of head trauma, and 60% had prior radiation exposure, factors which may have contributed to the onset of glioblastoma (Figures 5,6).





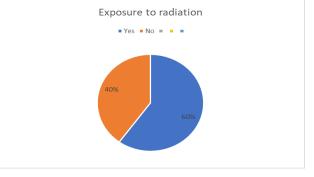


Figure 5 :Distribution of Patients According to Radiation Exposure

F. Clinical Symptoms

A wide range of symptoms were reported among glioblastoma patients. Memory disorders were the most prevalent (Figure 7), observed in 86% of patients, followed by vision problems in 70% (Figure 8). Speech difficulties were relatively rare, affecting only 10% of the patients (Figure 9). Notably, 100% of the patients experienced nausea and vomiting (Figure 10), as well as headaches (Figure 110), which are hallmark symptoms of increased intracranial pressure caused by tumor growth. Movement difficulties were reported in 40% of patients (Figure 12), while urinary incontinence was a rare symptom, affecting just 3% (Figure 13). Interestingly, no patient experienced seizures following diagnosis (Figure 14), which is somewhat unusual for brain tumors.

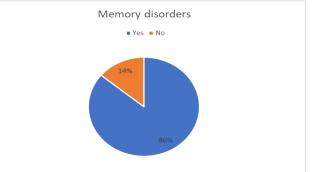


Figure 6 :Patients were Distributed According to Memory Problems

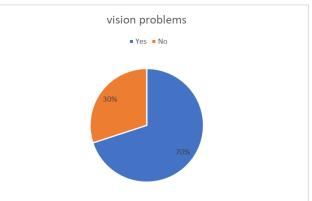


Figure 7:Patients were Distributed According to Exposure to Vision Problems

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Figure 8 :Patients were Distributed According to Exposure to Speech Problems

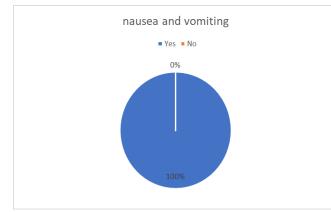
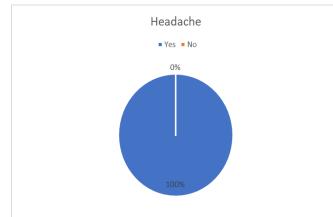


Figure 9: Patients were Distributed According to Exposure to Nausea and Vomiting



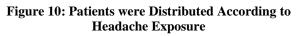




Figure 11: Distribution of Patients According to Movement Difficulties

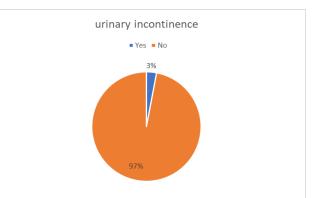


Figure 12: Distribution of Patients According to Urinary Incontinence

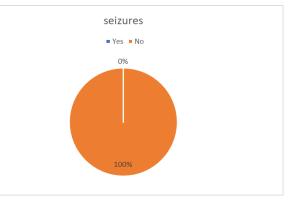


Figure 13: Patients were Distributed According to Exposure to Epileptic Seizures

G. Tumor Type

The predominant type of glioma diagnosed in this cohort was astrocytoma, accounting for 70% of cases. Other glioma types included ependymal tumors (20%) and oligodendrogliomas (10%). These distributions align with global data on glioma subtypes, where astrocytomas are the most common (Figure 15).

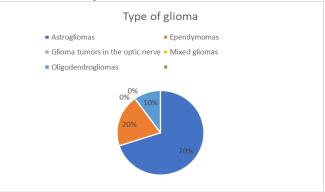


Figure 14: Distribution of Patients According to the type of Glioma

H. Diagnostic Methods

The majority of patients (76%) were diagnosed using nuclear magnetic resonance imaging (NMR) with contrast, which is the gold standard for identifying gliomas. The remaining 24% were diagnosed via CT scans with contrast, which is often used when NMR is unavailable or contraindicated (Figure 16).

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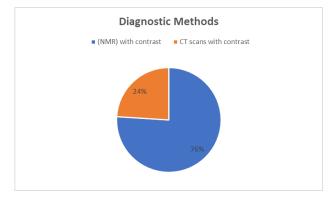


Figure 15: Distribution of Patients According to Diagnostic Method

I. Treatment Methods

The treatment protocols followed at Tishreen University Hospital were primarily multimodal. 80% of patients underwent a combination of surgery, radiation therapy, and chemotherapy. The remaining 20% received only surgery and radiation, either due to contraindications for chemotherapy or patient choice. The surgical resection aimed for maximum tumor debulking, while radiation and chemotherapy were used to control residual tumor growth (Figure 17).

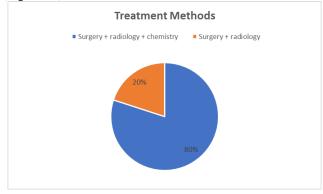


Figure 16: Distribution of Patients According to Treatment Type

J. Genetic History

Interestingly, only 6% of the patients in this cohort reported a family history of genetic predisposition to cancer. The remaining 94% had no such history, suggesting that in most cases, glioblastoma arises sporadically rather than being inherited. This highlights the need for further research into environmental and lifestyle factors that may contribute to the development of this malignancy (Figure 18).



Figure 17: Distribution of Patients According to Genetic History in the Family

K. Treatment Relapse

A significant challenge in glioblastoma treatment is patients' post-treatment relapse. In this study, 26% of patients experienced a recurrence of the tumor after their initial treatment. The average duration of remission before relapse was approximately four months, emphasizing the aggressive nature of glioblastoma and its tendency to recur quickly after treatment, despite multimodal interventions (Figure 19).

Throughout the follow-up period, only four out of the 30 glioblastoma patients included in the study passed away.

This study's findings highlight the complexity of glioblastoma treatment and the numerous factors that influence patient outcomes, from age and lifestyle habits to the choice of treatment modalities. The insights gained here could contribute to refining therapeutic approaches and improving prognosis for glioblastoma patients, particularly in resource-limited settings like Syria.

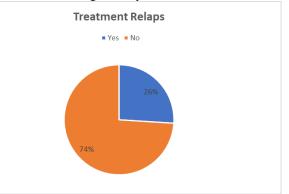


Figure 18: Patients were Distributed According to the Incidence of Recurrence After Treatment

V. DISCUSSION

The findings from this study provide important insights into the clinical and demographic characteristics of glioblastoma patients treated at Tishreen University Hospital. One of the most notable results was the age distribution, with a significant portion of patients being younger than what is typically reported in global glioblastoma epidemiology [13]. In our cohort, 35% of the patients were under the age of 40, which contrasts sharply with data from Western populations, where the median age of diagnosis is typically around 64 years [14]. Studies from Europe and North America consistently indicate that glioblastoma is primarily a disease of older adults, often diagnosed in individuals aged 55 and above [15].

A plausible explanation for this younger age distribution in our study could be environmental and genetic factors specific to the region. One particularly relevant factor is prior exposure to radiation, which was reported in 60% of the patients in our cohort. Radiation exposure, particularly in regions affected by conflict, has been well-documented as a risk factor for the development of gliomas and other brain tumors [16].

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Syria has experienced significant conflict over the past decade, which may have led to increased environmental radiation exposure due to damage to industrial and medical facilities that use radioactive materials [17]. Additionally, prolonged stress associated with conflict may also contribute to earlier onset of disease. Stress has been shown to affect the immune system, potentially impacting the body's ability to fight off the initial cellular mutations that could lead to cancer [18]. In comparison, studies conducted in regions without such environmental stresses tend to report glioblastoma primarily in older adults. A study conducted by Ostrom et al. (2016) in the United States found that the median age of diagnosis was 64 years, and only a small fraction of patients were under the age of 40 [19]. This highlights the possible influence difference of environmental factors and supports the need for further research into how the Syrian conflict may have contributed to the earlier onset of glioblastoma observed in our study.

Another significant finding was the high proportion of male patients (63%) compared to female patients (37%). This result is consistent with global data that show a male predominance in glioblastoma cases, with various studies reporting a male-to-female ratio of approximately 1.6:1 [13]. The reasons behind this gender disparity are still not fully understood, but several studies have suggested that hormonal differences and genetic factors may play a role. Estrogen is believed to have neuroprotective effects, which may offer some protection against the development of glioblastoma in females [20]. Additionally, some genetic studies have identified sex-linked differences in glioblastoma biology, with male patients more likely to exhibit certain genetic mutations associated with poor outcomes [21]. For instance, the EGFR (Epidermal Growth Factor Receptor) amplification and PTEN (Phosphatase and Tensin Homolog) deletion, both of which are common in glioblastoma, tend to occur more frequently in male patients [22].

The clinical symptoms observed in our cohort align closely with those reported in the broader literature. Memory disorders (86%) and vision problems (70%) were common, and all patients experienced headaches, nausea, and vomiting. These symptoms are consistent with glioblastoma's typical presentation due to the tumor's mass effect, which increases intracranial pressure and affects surrounding brain structures [23]. However, a notable divergence from the literature was the absence of postdiagnosis seizures, with 0% of our patients reporting this symptom. Studies such as that by Pallud et al. (2014) have shown that seizures occur in up to 50% of glioblastoma patients, particularly those with tumors located in the temporal lobe [24]. The absence of seizures in our cohort may be due to differences in the management of symptoms or variations in tumor location and biology. Alternatively, genetic factors unique to our population may play a role, and further investigation into the genetic profile of Syrian glioblastoma patients could provide additional insights [25].

Regarding tumor types, the predominance of astrocytomas in our study (70%) is consistent with global trends, where astrocytomas represent the majority of glioblastomas [26]. However, the relatively high incidence of ependymal tumors (20%) and oligodendrogliomas (10%) in our cohort warrants further investigation [26]. While these tumor types are less common than astrocytomas, they exhibit different biological behaviors and may have different treatment responses [27, 28]. Oligodendrogliomas, for example, tend to have a better prognosis due to their responsiveness to chemotherapy, particularly in patients with 1p/19q co-deletion. Ependymal tumors, on the other hand, are rarer but are associated with poor outcomes, especially when located in the brain rather than the spinal cord [27, 28]. The relatively high incidence of these tumor types in our cohort may be related to genetic predispositions or environmental factors unique to our region, and further studies are needed to understand the underlying causes.

In terms of treatment, our study found that 80% of patients received a combination of surgery, radiation therapy, and chemotherapy, which reflects the standard treatment protocol for glioblastoma worldwide [29]. Maximal surgical resection followed by adjuvant therapy remains the cornerstone of glioblastoma treatment, as it provides the best chance for prolonging survival [30]. However, the high relapse rate observed in our study (26%) and the short average remission period of just four months underscore the aggressive nature of glioblastoma and its resistance to conventional therapies [31]. Even with optimal treatment, glioblastoma has a notoriously poor prognosis, with a median survival of 12 to 15 months [32]. A study by Stupp et al. (2005), which introduced that the use of temozolomide in combination with radiation therapy significantly improved survival rates, but glioblastoma remains highly resistant to treatment, often due to its highly invasive nature and the presence of treatment-resistant cancer stem cells [33].

During the follow-up period, out of the 30 glioblastoma patients included in the study, only four patients passed away. This represents a mortality rate of approximately 13.3% over the six-month observation period. The relatively low number of deaths during this timeframe may suggest that the majority of patients were either responding to treatment or that the disease had not yet progressed to its terminal stages. Further analysis of these cases, including the treatment regimens and clinical factors associated with survival, will provide valuable insights into patient outcomes in this cohort.

In our study, the absence of targeted therapies and immunotherapies may have contributed to the poor outcomes observed. Recent advancements in glioblastoma treatment, such as the use of tumor-treating fields and checkpoint inhibitors, have shown promise in clinical trials, but these treatments were not available to most of the patients in our cohort due, as previously mentioned, to limited healthcare resources [34]. The availability of such novel therapies in resource-limited settings like Syria could potentially improve outcomes for glioblastoma patients in the future [35][36].

VI. CONCLUSION

In conclusion, this study offers valuable data on the demographic, clinical, and treatment-related characteristics of glioblastoma patients treated at Tishreen University Hospital.

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Our findings indicate a younger age distribution than typically observed in glioblastoma populations, as well as a notable male predominance. Common symptoms included memory loss, vision problems, and headaches, which are consistent with the literature. However, the absence of postdiagnosis seizures in our cohort is an intriguing deviation that requires further investigation. Treatment outcomes in our study were in line with global trends, with surgery, radiation, and chemotherapy being the primary treatment modalities. Despite these interventions, the relapse rate and short remission duration underscore the need for improved therapeutic options.

VII. LIMITATIONS

This study has several limitations. First, it is a retrospective analysis, meaning that data were collected from existing hospital records, which may introduce biases due to incomplete or inconsistent documentation. Second, the study was conducted at a single institution, which limits the generalizability of the findings to other regions or healthcare settings. Third, due to resource constraints, advanced molecular profiling of tumors was not performed, which could have provided a deeper understanding of the genetic factors influencing patient outcomes. Fourth,, the follow-up period was relatively short, which may have impacted the ability to assess long-term survival and relapse rates comprehensively. Finally, the sample size was relatively small, which may have affected the exactitude of certain results.

VIII. RECOMMENDATIONS

Based on the results of this study, several recommendations can be made for future research and clinical practice. First, there is a need for larger, multi-center studies to confirm the trends observed in our cohort, particularly the younger age of onset and the absence of post-diagnosis seizures. Second, incorporating advanced molecular profiling into routine diagnostic protocols could provide a more personalized approach to treatment, helping to identify patients who may benefit from targeted therapies or immunotherapy. Third, efforts should be made to improve access to newer treatment modalities, particularly in resource-limited settings like Syria. Finally, the high relapse rate observed in our study highlights the need for better post-treatment monitoring and the exploration of novel therapeutic options to prevent tumor recurrence.

IX. ACKNOWLEDGEMENT

We would like to express our sincere gratitude to the staff and healthcare professionals at Tishreen University Hospital for their invaluable support in facilitating this research. Special thanks go to the neurology and oncology departments for their assistance in data collection and patient care. We also extend our appreciation to the patients and their families, whose willingness to participate in this study made it possible. We acknowledge the contributions of the statistical team at Tishreen University for their help in analyzing the data.

DECLARATION STATEMENT

After aggregating input from all authors, I must verify the accuracy of the following information as the article's author.

- Conflicts of Interest/ Competing Interests: The authors declare that this study was conducted following all ethical standards and received approval from the ethics committee of Tishreen University and Tishreen University Hospital. All patient data were anonymized, and informed consent was obtained from each participant prior to inclusion in the study. The authors also declare no conflicts of interest related to this research.
- **Funding Support:** This article has not been funded by any organizations or agencies. This independence ensures that the research is conducted with objectivity and without any external influence.
- Ethical Approval and Consent to Participate: The content of this article does not necessitate ethical approval or consent to participate with supporting documentation.
- Data Access Statement and Material Availability: The adequate resources of this article are publicly accessible.
- Authors Contributions: The authorship of this article is contributed equally to all participating individuals.

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AUTHORS PROFILE



Dr. Rama Ibrahim. Doctor of Philosophy (PhD) in "Biochemistry, Cellular and Molecular Biology" from the Faculty of Medicine of the University of Paris (11)– France. Master's degree in "Cellular Physiopathology, Biotherapies and Diagnostic Innovations" from the Faculty of Pharmacy of the University of Paris (11)–

France. Diploma in "Pharmacy and Pharmaceutical Chemistry" from the Faculty of Pharmacy of Tishreen University–Syria. Professor of General and Clinical Biochemistry, Molecular Biology and Chemical Pathology at the Faculty of Pharmacy of Tishreen University-Syria. Professor of Clinical Biochemistry and Biotechnology at the Faculty of Pharmacy of Al-Sham Private University (ASPU)–Syria. Dean of the Faculty of Pharmacy of Al-Sham Private University (ASPU) – Syria (2019-2021). Member of the Quality Assurance Unit of the Faculty of Pharmacy of Al-Sham Private University (ASPU) – Syria.



Zein Al-Abideen Douba, Master's degree in Laboratory Diagnostics from the Faculty of Pharmacy, Tishreen University, Bachelor's degree in Pharmacy and Pharmaceutical Chemistry from the Faculty of Pharmacy, Alandalus University (2019-2024). Bachelor's degree in "Pharmacy" from the Faculty of Pharmacy of Tishreen

University–Syria (2018). Instructor of Pharmaceutical Sciences at the Faculty of Pharmacy of Tishreen University–Syria and the Faculty of Pharmacy of Al-Andalus University–Syria, with five years of teaching experience. Extensive internship experience at the Laboratories of Tishreen University Hospital and the Department of Oncology and Chemotherapy–Syria (2019-2021). Editor and Reviewer for the Open Access Journal of Oncology (OAJOY). Reviewer for the Asian Pacific Journal of Cancer Prevention and the Syrian Journal of Cancer Research. Assistant Editor of the Syrian Journal of Cancer Research. Active participant in the Syrian Expatriate Researchers Conference 2024, the most significant scientific forum in Syria. Published two peer-reviewed articles and submitted two more currently under review. One preprint available on SSRN.



Reema Khaddam, A Pharmacist Driven by Service and Education As a recent graduate of Pharmacy from Al-Sham Private University (ASPU), class of 2024, I am driven by a deep commitment to serving my community through healthcare and education. My passion for these areas is reflected in my diverse experiences, which have

allowed me to hone my skills and gain invaluable insights. My academic journey at ASPU culminated in a Bachelor of Pharmacy degree, equipping me with a comprehensive understanding of pharmaceutical principles and practices. Beyond my core studies, I actively sought out opportunities to further enhance my skills, completing courses such as Clinical Skills (2020), First Aid (2023), and Pharmacist Training (2021). These courses have broadened my knowledge base and equipped me to provide highquality patient care. Furthermore, I possess strong administrative capabilities, demonstrated by my proficiency in Excel, Word, and accounting software. My fluency in both Arabic and English enables me to communicate effectively with diverse individuals and navigate diverse healthcare settings. My professional experience includes three years of working in a community pharmacy (2021-2023), where I honed my patient counseling skills and gained experience in managing pharmacy operations. Simultaneously, I served as Language Lab Manager at ASPU (2022-2024), demonstrating my leadership abilities and passion for education. This role allowed me to foster a supportive learning environment and empower students to reach their full potential. Beyond my professional endeavors, I am dedicated to making a positive impact within my community.

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I actively participated in post-earthquake relief efforts and volunteer with the organization "Utopians," demonstrating my commitment to serving others and promoting community well-being. My strong communication skills, adaptability, and unwavering passion for service make me a valuable asset to any organization seeking a dedicated and skilled individual. I am eager to contribute my expertise and enthusiasm to a team committed to improving the health and well-being of our community.



Haider Mohammed Ibrahim, I am Haider Mohammed Ibrahim, a recent graduate of Pharmacy from the Private University of Sham (PUS), class of 2024. Born and raised in Jablah, Ain Shaqaaq, I possess a deep commitment to serving my community through healthcare. My academic journey at PUS culminated in a Bachelor of Pharmacy

degree, equipping me with a strong foundation in pharmaceutical knowledge and practice. I am also have completed an ICDL course in 2022, enhancing my computer skills and preparing me for the technological demands of modern pharmacy. My intermediate proficiency in English allows me to communicate effectively in diverse healthcare settings. During my time at PUS, I gained valuable practical experience through working in a community pharmacy from 2022 to 2024. This experience provided me with firsthand knowledge of patient counseling, pharmacy operations, and the importance of building positive relationships with patients.I am a dedicated and ambitious individual driven by a strong work ethic and a passion for serving my community. I am constantly seeking opportunities to learn and develop my professional skills, ensuring I remain at the forefront of the ever-evolving healthcare landscape. My commitment to patient well-being, coupled with my academic achievements and practical experience, make me a valuable asset to any organization seeking a motivated and skilled pharmacist. I am eager to contribute my expertise to a team committed to delivering high-quality healthcare services. For inquiries.



Bassam Solaiman Saad, MD, PhD, Nuclear Medicine and Radiation Oncologis Assistant Professor, Head of the Department of Oncology at Tishcreen University Hospital in Latakia, Syria Responsible for oncology education of undergraduate medical students at the faculty of medicine, and supervisor for postgraduate

program in radiation oncology and nuclear medicine. Member of Syrian society of oncology. Main research interest is the malignancies of central nervous system which study the post-surgical adjuvant treatment modalities which include the radio – chemo-and targeted therapy. Our department cover the north and costal region of Syria. Another duties include patients care of all malignancies.

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