



Cancer Diagnoses during Active Conflict: Experience from a Cancer Program in Northwest Syria

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Abstract

Background Protracted conflict has destroyed Syria's health system with severe impacts on the diagnosis and treatment of chronic and high-cost diseases including cancer. Here, we review the type and (where possible) the stage of cancers diagnosed in a pathology laboratory serving Northwest Syria.

Methods We retrospectively reviewed all pathology reports which reported a diagnosis of cancer from a pathology department in Northwest Syria from January to December 2020.

Results A total of 397 new cancers were diagnosed during 2020 of which 191 were among males (48.1%) and 20 cases were in children aged 17 years or under (5%). The most common cancer in men was bladder cancer (15.7%) and skin cancers (14.7%) followed by cancers in the lymph nodes (includes primary and secondary; 9.9%). In women, breast cancer (38.3%) followed by skin cancer skin (9.7%) and uterine cancer (8.7%) was the most common. The overall proportion of cancer diagnoses were breast cancer (20.2%), skin cancer (12.1%), cancer affecting lymph nodes (8.8%), and urinary bladder (8.3%) and colorectal cancer (7.3%).

Discussion This preliminary analysis is the first report of cancer types and demographics in areas outside of government control in Syria since the onset of the conflict. Despite limitations, it presents some indication of the burden of oncological diagnoses in this area. Further research which aims to describe and address the burden of cancer on populations under ongoing conflict and humanitarian crises remains essential, especially in Northwest Syria given ongoing attacks and severe underfunding. There is a particular need to investigate how best to apply interventions and support health systems and cancer services within conflict settings. More support and resources need to be allocated to cancer centers with long-term health partnership models. The underresourced and understaffed conditions of the hospital are significant limits to a more detailed report.

Keywords

- ▶ cancer
- ▶ Syria
- ▶ conflict
- ▶ histopathology
- ▶ breast cancer

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Introduction

The diagnosis and management of cancer during protracted conflict present many challenges, as they require robust health systems. Syria's health system has been devastated by the conflict which has left less than 60% of health facilities functioning and driven the forced displacement of thousands of health care workers; this has included specialists including oncologists of which only 35 remain across Syria.¹ The health system itself is fragmented, leaving different regions under different geopolitical control with varied access to health care services, particularly for specialist services like oncology. Most oncology care has historically been concentrated in the major cities, including Damascus and Aleppo,² which are now under the control of the Syrian government. As such, areas outside of government control, including Northwest Syria, have insufficient provision of oncology care.³ As of the last quarter of 2020, this area had three oncology centers with access to six computed tomography (CT) scanners and three magnetic resonance imaging (MRI) machines among them.⁴

Oncology services in Northwest Syria are insufficient to meet the needs of the 4.17 million who reside in this area, half of whom are internally displaced people (IDP).³ Around 80% of IDP are women and children. Given continued hostilities with attacks on Northwest Syria by the Syrian government and its allies, including against health care facilities, access to health care is interrupted. This is particularly so for costly or specialist interventions including oncology care. The withdrawal of the Syrian Ministry of Health from the Northwest Syria early in the conflict left a gap in health and humanitarian services; this has been filled by Syrian and international humanitarian organizations.⁵ Many of these have been reluctant to provide costly services, given the vast health and humanitarian needs in the area alongside insufficient funding. However, given the needs, some humanitarian organizations, including the Syrian American Medical Society (SAMS), a U.S. and Turkey registered organization stepped in to support oncology care in the area with funding, training, and resources. SAMS' oncology center was established in Idlib city in 2018 to provide oncology care.⁶ In 2020, SAMS established another oncology center in Al Bab primary health care center and a further one in Jarablus city. It also supported the provision and improvement of histopathology services in Al-Rai Hospital in Northwest Syria to support oncology care.⁷

National reporting on cancer is made to the International Agency for Research on Cancer–Global Cancer Observatory (IARC-GLOBOCAN). However, given the fragmented health system in Syria and the withdrawal of the ministry of health from areas under opposition control, soon after the onset of the conflict, national level reporting often excludes reporting from Northwest Syria. As such, IARC-GLOBOCAN data report on areas under government control. The aim of this research study is to describe the main oncological diagnoses of patients seen in a hospital serving the Northwest Syria between January 1, 2020, and December 31, 2020, as a baseline to understand the burden of cancer in this area.

A secondary aim is to compare how the proportions of different cancers (as reported histologically) compared with national reporting from Syria.

Methods

This study retrospectively identified cancer histopathology reports from the pathology department serving Northwest Syria between January and December 2020; these had been routinely collected for clinical purposes. From these reports, demographic data, type of cancer, and stage of disease (where available) were recorded and analyzed in Excel. Relative percentages of different cancers were compared with the IARC-GLOBOCAN data for the whole of Syria.

Setting

The Al-Rai pathology laboratory within the hospital is located in Northern Aleppo governorate; it is supported by the Turkish Ministry of Health and receives biopsy samples from eight public and private hospitals in the local area including the cities of Azaz, Albab, Jarablus, Marea, and Al-Rai.

Participants

Anonymized data relating to clinical histopathological samples from patients diagnosed with cancer are included. This is a noninterventional study, and no patient identifiable details were collected.

Variables

Variables of interest included demographic data, site and type of sample, type of cancer, stage of disease (where available).

Data Sources and Study Size

Data were obtained from the histopathology laboratory of Al-Rai Hospital in Northwest Syria. All data were anonymized and only provided to limited members of the research team to be able to analyze the data. All samples were included during the study period.

Statistical Methods

Data were analyzed in Excel and descriptive statistics was used to describe the percentages in adults and children of different cancers based on the histopathological findings. These were then compared with data from IARC-GLOBOCAN which gives number and percentages of cancer diagnoses in areas under government control in Syria. This is primarily a descriptive study; as such, no statistical tests were performed.

Bias

All data were obtained from a single laboratory supported by SAMS; however, it received samples from several facilities in the area. The histopathology reports may not be truly representative of actual cancer rates in the area as patients who are not sampled, either if they are too unwell or if there is insufficient expertise, for example, lung biopsies would not be represented. A further skew includes the fact that

patients with cancer or suspected cancer in Northwest Syria may not all present to this facility and may choose, if possible, for them to go to areas under government control or Turkey for oncological diagnosis and care. As such, this could skew the numbers and proportions of different cancers.

Ethics Statement

Anonymized data were provided by Al-Rai oncology center and had been collected solely for clinical purposes. As such, formal ethics approval was not sought but was approved by the SMAS's research committee.

Results

A total of 1,654 pathology specimens were recorded in a pathology department and cancer was diagnosed in 397 (24%) reports: 191 (48.1%) males and 20 (5%) children of aged 17 years or under. The most common sites were breast (20.2%) followed by skin (12.1%), lymph nodes (8.8%), urinary bladder (8.3%), and colorectal cancer (7.3%). Among females, breast cancer was the most common cancer, accounting for 38.3% of cancers diagnosed followed by skin (9.7%) and uterine (8.7%). Among males, bladder cancer was the most common (15.7%) followed by skin (14.7%) and lymph nodes (9.9%).

Breast Cancer

Breast cancer was diagnosed in 80 cases (20.2% of total) of which one case was male. Diagnoses included invasive ductal carcinoma (60), invasive lobular carcinoma (10), breast primaries seen in lymph nodes (4), mucinous carcinoma (2), ductal carcinoma in situ (2), undifferentiated sarcoma (1), and medullary carcinoma (1). Also, 34 cases were diagnosed after mastectomy of which 22 cases were recorded as at least stage III; however, there was no further data regarding follow-up with imaging or other diagnostic methods to identify metastasis, therefore some cases may have been stage IV.

Cancer Affecting Lymph Nodes

Overall, 35 cancers (8.8% of total) were identified in lymph nodes of which 19 cases were metastatic cancers for which 10 had primary sites identified. Metastatic tumors accounted for 11% of all cases with the primary source identified in 10 cases of which 4 were breast primaries, 2 were papillary carcinomas of the thyroid gland, 1 was a small cell carcinoma of the lung, 1 was a seminoma, and 2 were squamous cell carcinomas; nine were from an unknown primary. Nineteen cases were in males and 16 in females with a mean age of 52 years. Of the remaining 16, 8 were Hodgkin's lymphoma and 8 were non-Hodgkin's lymphoma.

Skin Cancer

Of the 48 samples (12% of total), the most common findings were: squamous cell carcinoma (26), basal cell carcinoma (20), malignant melanoma (1), and dermatofibrosarcoma protuberans (1).

Bladder Cancer

Bladder cancer accounted for 33 cases (8.3% of the total); 23 of the cases were diagnosed through transurethral resection of the bladder tumor (TURBT). Also, 16 cases were staged as high grade, 8 of which invaded surrounding muscles.

Colorectal Cancer

Colorectal cancer accounted for 29 cases (7.3% of the total). Cases were diagnosed through endoscopic biopsies and colectomies. Adenocarcinoma was the most common colorectal malignancy (24 cases), followed by mucinous adenocarcinoma (4 cases) and one gastrointestinal stromal tumor. In the 18 colectomy samples received, 6 were at least stage III, one case was of stage IV (with liver metastasis), and the remainder cases were of stages I and II.

Cancer in Children

Of the 20 cases of cancer diagnosed in children aged 17 years and under, there was one case each of rhabdomyosarcoma, dermatofibrosarcoma protuberans, sarcoma of the small intestine, malignant teratoma, metastatic neuroblastoma, and a yolk sac tumor. There were four cases of renal cancer (two renal cell carcinomas, one low grade papillary carcinoma, and one congenital mesoblastic nephroma). There was one case of ganglioneuroblastoma in the adrenal gland. There were three cases of brain cancer, two were pilocytic astrocytomas (WHO grade I) and one case of a classical medulloblastoma in the cerebrum (WHO grade IV). There were two cases of retinoblastomas, two bone cancers (one giant cell tumor and one Ewing's sarcoma) and two cases of non-Hodgkin's lymphoma (one case identified by lymph node and one case in the bone marrow).

Miscellaneous

In addition to the cancers outlined previously, other cancers (inclusive of both adults and children) reported, accounting 129 samples (32.4% of total). These cancers include the following: bone (11 adults and 2 children, 3.3% of all cases), laryngeal (13 adults, 3.3%), soft tissue (13 adults, 3.3%), liver (9 adults, 2.3%), lung (10 adults, 2.5%), ovary (8 adults and 1 child, 2.3%), stomach (9 adults, 2.3%), bone marrow (6 adults and 2 children, 2%; of which 5 cases showed atypical lymphocytes, 1 showed metastasis with a primary neuroblastoma, 1 showed plasmacytoma from multiple myeloma, and 1 metastatic adenocarcinoma of an unknown primary), kidney (4 adults and 4 children, 2%), testis (5 adults and 1 child, 1.5%), thyroid (8, 2%), cervix (5, 1.3%), brain (1 adult and 3 children, 1%), mediastinum (4 adults, 1%), pancreas (4 adults, 1%), peritoneum (3 adults, 0.8%), esophagus (2 adults, 0.5%), mandible and maxilla (2 adults, 0.5%), nasal cavity (2 adults, 0.5%), small intestine (1 adult and 1 child, 0.5%), and gallbladder (1 adult, 0.3%) cancers.

► **Table 1** compares the percentages of cancers identified from the Northwest Syria data to the common cancers in Syria reported by the IARC to GLOBOCAN; the latter contains reports from areas under the control of the government but excludes areas in Northwest Syria under opposition or Turkish control who do not report into this mechanism.

Table 1 Summarizes the main findings from this study alongside a comparison from the IARC at the WHO⁸; the latter is mainly from areas under the control of the Syrian government during 2020

	IARC WHO Fact sheet on Syria <i>n</i> (%)	Northwest Syria study <i>n</i> (%)	Relative difference (%)
Total (<i>n</i>)	20,959	397	
Female cases	11,716 (55.9)	191 (51.9)	-4
Male cases	9,243 (44.1)	206 (48.1)	+4
Childhood cases (0–17 years)	N/A	20 (5)	
Cancer type			
Breast cancer	4,388 (20.9)	80 (20.2)	-0.7
Lung cancer	1,976 (9.4)	10 (2.5)	-6.9
Colorectal	1,761 (8.4)	29 (7.3)	-0.9
Prostate	1,083 (5.2)	15 (3.8)	-1.4
Bladder cancer	955 (4.6)	33 (8.3)	+3.7
Bladder cancer in males	751 (8.1)	30 (15.7)	+7.6
Corpus uteri	489 (2.3)	18 (4.5)	+2.2
Cervix uteri	215 (1)	5 (2.4)	+1.4
Skin	-	48 (12.1)	-
Lymph node	-	35 (8.8)	-
Other cancers	-	129 (32.4)	-

Abbreviations: IARC, International Agency for Research on Cancer; N/A, not available; WHO, the World Health Organization.

The Northwest Syria data have a lower proportion of breast, lung, colorectal, and prostate cancers and a higher proportion of bladder cancers, uterine, and cervical cancers when compared with GLOBOCAN data.

Discussion

This is the first report on the proportions of different cancers (as noted on histological samples) diagnosed outside of the control of the Syrian government since the onset of the conflict. Our data shows that the most reported cancers in this center are breast (20.2% of total), skin (12%), lymph node (8.8%), bladder (8.3%) and colorectal cancer (7.3%). It is noted that IARC data do not include skin or lymph node cancers, and our data did not include hematological cancers. When comparing the percentages of cancers from that reported by IARC and Northwest Syria, we note that the largest discrepancy is among lung cancer patients with a proportion of 9.4 and 2.5%, respectively, and a 7.6% higher proportion of bladder cancer in males in Northwest Syria.

For lung cancer, the lower proportion in Northwest Syria could relate to under diagnosis given poor access to CT scans, as well as biopsy (which may be more complicated than that for other cancers), and generally poorer access to health care given ongoing bombardment in the area. The reason for the higher proportion of bladder cancers among males in Northwest Syria compared with the rest of Syria is uncertain. One suggestion is around the availability of a specialist surgeon who can carry out TURBT procedures coupled with the pathology laboratory's capacity to stain for bladder malig-

nancies. However, given population movements (for those able to travel) between areas under government control and those outside and the availability of specialists in areas under government control, this may not be the main explanation. Smoking is a risk factor for both bladder⁹ and lung cancers,¹⁰ but it is unlikely that smoking rates would differ between Northwest Syria and the rest of the country. However, smoking rates may have increased during the conflict.¹¹ There is also concern that given the higher proportion of attacks which have occurred in Northwest Syria compared with other parts of the country that there may have been a higher exposure to carcinogens.^{12,13}

There are little data on diagnostic delays in Syria; however, a study among Syrian refugees in Jordan noted that 65% presented with metastatic disease and as a result received delayed and suboptimal treatment.¹⁴ A study from Konya province in Turkey reported on 230 adult and 38 children who are Syrian refugees diagnosed with cancer between 2005 and 2020.¹⁵ They noted that 40% of patients had metastatic cancer at diagnosis. Of concern, they reported an overall survival probability of 37.5% at 5 years for adults in this study. This reinforces the importance of timely access to diagnosis and treatment, as well as public health measures to manage risk factors.

In this descriptive study, it is hard to ignore the effects which geopolitical changes have on health care access to oncology services. Part of Northwest Syria is under Turkish military control with the health system in this area following that of the Turkish health system; this includes Al-Rai, Jarablus, and other areas close to the Turkish border.¹⁶ This increases the

complexity of providing oncology care in this area as well of effective public health interventions for populations in this Northwest Syria. Regarding cancer, this is pertinent given the importance or preventative measures, for example,, smoking cessation and the potential exposures related to weaponry used in the conflict including chemical weapons.¹²

Strengths and Limitations

Despite limitations, this study adds to sparse literature on cancer epidemiology in Northwest Syria. This manuscript describes cancers which have been histologically confirmed; this presents a bias and does not necessarily represent the true burden of different cancers in this population; this is particularly so for harder to biopsy cancers including lung cancer. Provision of cancer services by SAMS in the three oncology centers in Northwest Syria are free of charge; however, there are associated costs and distances of travel which could preclude some patients from travelling to the centers; this may also skew the data. Additionally, even if patients present to health care, they may not be well enough or there may not be the right skills available for some of the more invasive histological diagnoses which will also present a bias in the data. Data presented are from Al-Rai pathology laboratory which received samples from three oncology centers in Northwest Syria, as such it may not be representative of other areas. Also, patients in Northwest Syria who have the means, may choose to seek care in areas under government control including Damascus or Turkey if they are able though for others, security risks may preclude this.

Further work should include the collection of clinical data alongside the histopathology reports including duration of symptoms, other diagnostics, for example, imaging will further elucidate information on cancer patients in Northwest Syria. Other details which could support planning include the geographical origin of patients accessing cancer care at the center and distance of travel.

Conclusion

With this analysis, we hope to stimulate discussion on the importance of oncology care during protracted conflict with the need for improved diagnostics (including histopathology and imaging) and the support of oncologists through training and career progression. This has been provided by some humanitarian organizations; however, further capacity is required for the timely diagnosis of cancers to support improved outcomes in such complex humanitarian settings.

Authors' Contributions

B.A., A.T., M.H., and A.A. conceived the concept. B.A., G.T., H.M., and A.A. prepared the first draft and contributed significant to revisions. G.T. and H.M. supported data analysis. J.D., A.J., M.K., Y.A., M.A., M.H., and A.T. contributed to significant revisions of the manuscript and provided suggestions around key points to include.

Conflict of Interest

None declared.

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