

Pattern of cancers in adolescent and young adults. A 15-year retrospective study at King Fahad Hospital, Al-Madinah Al-Munawwarah, Saudi Arabia

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ABSTRACT

Objectives: To evaluate the incidence and pattern of cancer in adolescents and young adults (AYAs) age group in Al-Madinah Al-Munawwarah region of Saudi Arabia.

Methods: This retrospective histopathology-based study was conducted at a tertiary care center in Al-Madinah Al-Munawwarah, Saudi Arabia and comprised cases of cancers for 15 years between January 2006 and December 2020.

Results: During the last 15-year period, 8,769 cases of cancers were diagnosed out of which 475 (5.4%) cases were registered in AYAs. Of these cases, 232 (48.8%) were males while 243 (51.2%) were females, with a male-to-female ratio of 0.9:1. The 3 most common cancer groups in the entire cohort were carcinomas (n=165; 34.7%), lymphomas (n=135; 28.4%), and leukemias (n=91; 19.2%). The most common sites in carcinomas were thyroid (n=60; 12.6%), breast (n=35; 7.4%), and gastrointestinal (n=18; 3.8%). The leading cancers in males were the lymphomas (n=74; 15.6%), leukemias (n=57; 12%), bone (n=21; 4.4%), and central nervous system (n=20; 4.2%), while in females, the most common cancers were the lymphomas (n=61; 12.8%), thyroid (n=40; 8.4%), breast (n=34; 7.2%), and leukemias (n=34; 7.2%).

Conclusion: Our findings are in concordance with studies in national and international literature and we believe that our study provides a baseline tool for future population-targeted studies.

Keywords: adolescents, young adults, cancer, Madinah

*Saudi Med J 2021; Vol. 42 (4): 449-453
doi: 10.15537/smj.2021.42.4.20210028*

Although, the incidence of cancer in adolescents and young adults (AYAs) is lower than that of the elderly, it would still constitute a significant burden as patients of this age group are usually confronted with unique

physical, psychological, and social challenges, such as fertility, education, career, and late and long-term effects of treatment.¹ However, little attention has been paid by the healthcare professionals and policymakers toward this population.² This could be attributed to several factors, perhaps the most important one is the lack of an established definition for AYA. For instance, the US Surveillance Epidemiology and End Results (SEER) program defines AYA as those aged 15-39 years, while the United Kingdom (UK) and the EURO CARE (a European multinational project to examine cancer survival) study defines AYA as those aged 15-24 years. According to the Canadian Cancer Society, AYA was defined as those aged between 15 and 29 years.³⁻⁵ In Saudi Arabia, there is no official age range definition for AYA even though the adolescents and young adults represents a large percentage of the population pyramid. The most recent national census showed that there were 7,710,517 residents of the age-group 15-29 years in 2016, accounting for 24.3% of the total population of Saudi Arabia.⁶ The Madinah region had a population of 2,080,436 at the last census of 2016, which represents 6.5% of the total population of Saudi Arabia and ranks the Madinah region as the fifth most populated region after the Makkah, Riyadh, Eastern, and Aseer regions. There were 493,082 residents of the age-group 15-29 years in the Madinah region which is accounting for 6.4% of the total young Saudi population.⁶

An extensive search in the published literature revealed a paucity of reports on the incidence and pattern of cancer in AYA in Saudi Arabia, particularly in the Madinah region. Thus, the aim of our study is to retrospectively evaluate the incidence and pattern of cancer in AYA age group in Al-Madinah Al-Munawwarah, region of Saudi Arabia.

Methods. In this study, we adopted the definition for AYA as those aged between 15 and 29 years. This retrospective study included 475 cases of cancers in AYAs between January 2006 and December 2020 diagnosed at the histopathology laboratory of the King Fahad Hospital (KFH), Al-Madinah, Saudi Arabia. King Fahad Hospital is a leading referral and tertiary care provider institute with 500 bed capacity. It is the main oncology hospital in the Al-Madinah region and majority of the cancers are diagnosed and treated in KFH. All patients

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

with histopathological-proven primary cancers were included. Demographic characters including age, gender, nationality, and diagnosis was retrospectively retrieved from the laboratory computer database. The present study was a retrospective study, and did not involve any patient's personal information. Hence, according to the principles of Helsinki Declaration, no ethical approval was required in our study.

Cancers are coded and classified based on the International Classification of Diseases for Oncology (ICD-O) and grouped further according to the most common types of cancers according to the Birch classification.⁷ The medical records were reviewed carefully for each patient including the present and past medical history, and CT scan, MRI, and PET scan were investigated to rule out the presence of any tumor in the past in such a manner that the metastatic cancers could be excluded from this study. As the main aim of the study was to address the basic demographic and histopathological information of cancers in AYAs, and no comparison was indicated between the parameters; hence, no statistical analysis was performed. Please arrange the references number in numerical order

Results. During the last 15-year period, 8,769 cases of cancers were diagnosed at KFHC, out of which 475 (5.4%) cases of primary cancers were registered in AYAs. The number of metastatic cancers in AYAs were 6 (breast: n=2, papillary CA thyroid: n=1, follicular carcinoma thyroid n=1, small cell CA lung n=1 and colorectal CA n=1). However, these metastatic cancers were not included in the study. The Birch classification subgroups of cancers in AYAs with their frequencies, and age distribution in 3 sets of age groups were mentioned in **Table 1**. Of these cases, 232 (48.8%) were males while 243 (51.2%) were females, with a male-to-female ratio of 0.9:1. There were 133 (28%) patients in the 15-19 years age group, 144 (30.3%) in 20-24, and 198 (41.7%) in 25-29. The 3 most common cancer groups in the entire cohort were carcinomas (n=165; 34.7%), lymphomas (n=135; 28.4%), and leukemias (n=91; 19.2%). The most common sites in carcinomas were thyroid (n=60; 12.6%), breast (n=35; 7.4%), and gastrointestinal (n=18; 3.8%). The most prevalent cancers in younger AYA (15-19 years) were lymphomas (n=42; 8.8%), leukemias (n=34; 7.2), and bone (n=19; 4%). In contrast, older AYA (25-29 years)

Table 1 - Over all distribution of 475 tumors in adolescents and young adults (AYAs) as per Birch classification.

Classification Cancer	15-19 years		20-24 years		25-29 years		Total
	Males	Females	Males	Females	Males	Females	
Group 1							
Leukaemias (AML+ALL+Others)	27	11	16	9	14	14	91 (19.1)
Group 2 - Lymphomas							
2.1 NHL	6	2	8	7	11	8	42 (8.8)
2.2 HL	17	17	17	15	15	12	93 (19.5)
Group 3 - CNS tumors	4	1	8	1	8	4	26 (5.4)
Group 4 - Bone tumors	12	7	6	2	3	2	32 (6.7)
Group 5 - Soft tissue sarcomas	1	2	1	2	1	1	8 (1.6)
Group 6 - Germ cell tumors	1	1	2	1	3	1	9 (1.9)
Group 7 - Melanoma and skin carcinoma	1	1	3	1	4	3	13 (2.7)
Group 8 - Carcinomas except skin							
8.1 - Carcinoma of thyroid	2	6	4	17	4	27	60 (12.6)
8.2.1 - Nasopharyngeal carcinoma	3	2	3	2	2	1	13 (2.7)
8.3 - Carcinoma of lung	1	1	1	2	2	2	9 (1.9)
8.4 - Carcinoma of breast	0	1	0	6	1	27	35 (7.3)
8.5 - Carcinoma of genito-urinary tract	0	0	1	0	1	1	3 (0.6)
8.5.1 - Carcinoma of kidney	1	0	1	1	3	1	7 (1.5)
8.5.2 - Carcinoma of bladder	-	2	-	2	-	5	9 (1.9)
8.5.3 - Carcinoma of ovary							
8.6 - Carcinoma of gastrointestinal tract							
8.6.1 - Carcinoma of colon and rectum	0	0	1	1	4	5	11 (2.3)
8.6.2 - Carcinoma of stomach	1	1	1	1	1	2	7 (1.5)
8.6.3 - Carcinoma of liver	0	1	1	0	4	1	7 (1.5)

CNS: central nervous system, AML: acute myeloid leukemia, ALL: acute lymphoblastic leukemia

suffered mainly from lymphomas (n=46; 9.7%), thyroid (n=31; 6.5%), breast (n=28; 5.9%), and leukemias (n=28; 5.9%). The leading cancers in males were the lymphomas (n=74; 15.6%), leukemias (n=57; 12%), bone (n=21; 4.4%), and central nervous system (n=20; 4.2%), while in females, the most common cancers were the lymphomas (n=61; 12.8%), thyroid (n=40; 8.4%), breast (n=34; 7.2%), and leukemias (n=34; 7.2%). The analysis of few frequently noted questions was summarized in **Figure 1**. Our findings clearly indicate that there is a gradual increase in the total number of cases from 15-19 years age group to 25-29 years age group.

Discussion. The data on the pattern of cancers in the AYAs is scant in Saudi Arabia, rather an extensive search of literature revealed no published reports on the cancer in this strategically important age group from Saudi Arabia.⁸ However, an expanding knowledge of cancers in AYAs is available from many countries such as United States,^{3,9} Europe,⁴ Canada,⁵ Australia,¹⁰ the Netherlands,¹¹ Korea,¹² Lebanon,¹³ Brazil,¹⁴ India,² and Japan.¹⁵ The recent advances in the coordinated international research and newer treatment modalities in the pediatric cancer have led a remarkable improvement in the outcomes. However, cancers in AYAs have not benefited from similar efforts and this deficit has led the international researchers to focus more on this strategically important age group.⁹ The World Health Organization (WHO) has defined adolescent period from 10-19 years and youth as those with age from 15-24 years, while, the United States Surveillance Epidemiology and End Results (SEER) program have defined the AYAs as those aged between 15-39 year^{3,9} but, many other internationally recognized societies have define the AYAs population ranging in a range from 15-29 years.^{5,11-14} For better understanding of the cancers in AYAs we kept the age range from 15-29 years in our cohort.

Although, the present study was a retrospective and a single hospital-based research, yet, it can serve the purpose of providing the trends of AYAs with their basic demographic correlations which can be compared with the available research in the English literature. During the period of 15 years, a total of 475 cases of various cancers were reported in the AYAs which constitute 5.4% of total number of cancers diagnosed at KFH. The rate of cancer in AYAs in our cohort is higher than the reported number from Korea (2.3%),¹² Lebanon (2.9%),¹³ and Japan (3%).¹⁵ Sharma and Singh² from India reported 5.7% of cancers in AYAs which corresponds with our finding. Of these 475 cases, 232 (48.8%) were males while 243 (51.2%) were females, with a male-to-female ratio of 0.9:1, indicating a slight female preponderance. The female preponderance in our study corresponds to those of previous studies conducted in the United States of America,⁹ Netherlands,¹¹ Korea,¹² and Lebanon.¹³ The female predominance was mainly attributed

to the higher incidence of thyroid and breast carcinomas in these studies, similar observation was made in our study as well. Contrary to our observation of female preponderance, there are few studies from India reported a higher incidence of cancers in male AYAs. This higher incidence in male is mainly attributed to the male preference in India and some cancers such as lymphoma and leukemia are more common in males in their cohort.²

In this study, we divided the cancers in AYAs in 3 different age groups. As the international classification of childhood cancer is not appropriate for AYAs, Birch et al⁷ in 2002 proposed a new classification for this age group in accordance with the WHO for AYA and according to the International Classification of Diseases for Oncology (ICD-O). We also classified our observation of cancers in AYAs according to Birch classification and ICD-O.⁷

In our study, the most encountered individual cancer was lymphoma, which was observed in 28.4% (135/475) of cases for both gender and with not much differences between the different analyzed age groups. Barmant et al¹⁴ from Brazil and Scott et al⁹ from the USA in their study also reported similar finding of lymphoma being the frequently diagnosed cancer in AYAs. An interesting observation was noted in our study regarding the occurrence of various cancers in the different age group, we observed that AYAs age increased in the total number of cancers (**Figure 1**). There is an obvious difference in the type of cancers in young AYAs than the older AYAs. While lymphomas and leukemias were the most common cancers in the young AYAs, various epithelial carcinomas especially thyroid and breast carcinomas were more common in the older AYAs. This is mainly due to an increase in the occurrence of carcinoma in the older AYAs. The increased occurrence in carcinoma was primarily due to an increase rate of thyroid and breast carcinoma in the older AYAs, similar observations were noted in the United States,⁹ the Netherlands,¹¹ Korea,¹² and Brazil.¹⁴ It is primarily attributed to a rapid increase in the incidence of these malignancies in

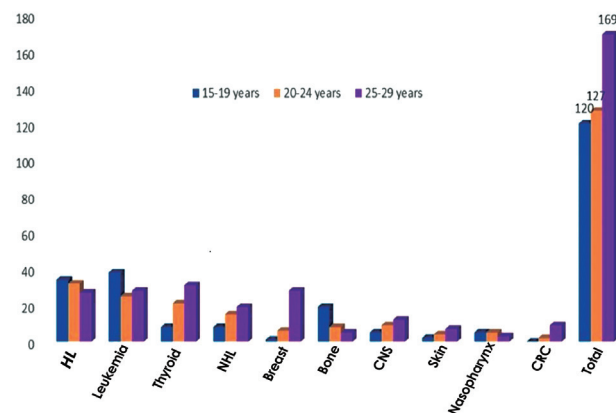


Figure 1 - Bar diagram representing the most frequently occurring cancers in our study with respect to the different age groups in the adolescents and young adults (AYAs). HL: Hodgkin lymphoma, NHL: non-Hodgkin lymphoma, CNS: central nervous system, CRC: colorectal cancer)

the older population and partially due to increase awareness and easy availability of screening tests and diagnostic facilities. However, the exact cause for the increased incidence of other cancers in AYAs is still unknown.^{9,12} We also observed that there is a decreasing trend in the relative incidence of leukemias, lymphomas, CNS tumors, bone, and soft tissue sarcomas and relative increase in the carcinomas as the age increases in the AYAs. Similar observations were reported by previous authors.⁹⁻¹¹ This shift may be attributed to many factors including hormone levels during puberty and pregnancy and exposure to environmental factors (late onset) versus genetic factors (early onset).⁹ Another contrasting

finding in our study was the incidence of melanoma which is lesser as compared to studies carried out in the US SEER³ Australia,¹⁰ and the Netherlands.¹¹ This could be attributed to chronic continuous sun exposure and increased melanin pigmentation in the majority of our people which acts as a natural sun protection factor. A detailed comparison of our findings of cancers in AYAs with the previously published literature is summarized in **Table 2**.

Study limitations. The absence of survival data that is mainly attributed to our patient selection from the histopathology laboratory rather than the medical record section. The retrospective nature of the study with lack of

Table 2 - Comparison of salient findings of cancers in adolescents and young adults (AYAs) in the present study with the previous published data in the English literature.

Authors and place of study	Type of study	Total number of cases	Male (%)	Female (%)	Cancers in AYAs with total cases (%)	Most common cancers in AYAs
Haggar et al ⁹ (2012) Australia	Population based	12,238	-	-	-	Melanoma Breast carcinoma Germ cell tumors Lymphoma
Aben et al ¹⁰ (2012) The Netherlands	Population based	23,161	51	49	-	Melanoma Germ cell tumor lymphoma Genitourinary tract carcinoma
Moon et al ¹¹ (2014) Korea	Hospital based	39,639	35.4	64.6	2.3	Thyroid carcinoma Lymphoma stomach carcinoma Breast carcinoma
Kourie et al ¹² (2014) Lebanon	Hospital based	205	49.5	50.5	2.9	Lymphoma CNS tumors Bone tumors Leukemia
Balmant et al ¹³ (2016) Brazil	Population based	-	51.5	48.5	-	Lymphoma Leukemias Melanoma Bone tumors
Sharma & Singh ² (2016) India	Hospital based	496	64.7	35.3	5.7	Head and Neck carcinoma CNS tumors GIT carcinoma Bone tumors
Inoue et al ¹⁴ (2017) Japan	Hospital based	86,494	35.1	64.9	3.1	Breast carcinoma Cervix and uterus carcinoma Thyroid carcinoma Colorectal carcinoma
Scott et al ⁸ (2020) United States	Eskiseher, Turkey	4,97,452	40.9	59.1	-	Breast carcinoma Lymphoma Thyroid carcinoma Melanoma
Present Study (2021) Saudi Arabia	Hospital based	475	48.8	51.2	5.4	Lymphoma Leukemias Thyroid carcinoma Breast carcinoma

CNS: central nervous system, GIT: gastrointestinal tract

age adjusted incidence rate. The lack of clinicopathological correlation with the chief complains, radiological findings, and staging of the cancers. Also, inclusion of some etiopathogenetic factors especially environmental exposure to a particular carcinogen in our cohort is also lacking. Lastly, the sample was restricted to one tertiary care government hospital, which might limit the extension of results to the general population.

In conclusion, the most common cancers in AYAs were lymphomas, leukemias, thyroid and breast carcinomas. There is an obvious difference in the type of cancers in young AYAs than the older AYAs. Population and hospital-based studies on cancers in AYAs are scarce and we believe that our study provides a baseline tool for future population-targeted studies. We strongly recommend further studies of the larger cohort at national and international levels to identify the etiological factors and better understanding of cancers in AYAs to improve the prognosis.

Acknowledgment. *The authors are thankful to Scribendi, the Editing and Proofreading Services for english documents (<https://www.scribendi.com>) for the English language editing services.*

Received 11th January 2021. Accepted 21st February 2021.

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