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Five Year Survival Rate of Adolescents and Young Adults (AYA) Cancer Patients: A Prospective Fixed Cohort Study in Bangladesh

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Authors' contributions

This work was carried out in collaboration among all authors. Author AAMK designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author PSA and Author MJA managed the analyses of the study. 'Author C' managed the literature searches. All authors read and approved the final manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Survivors of adolescent and young adult cancers (AYA) often live 50 to 60 years beyond their diagnosis. Cancer incidence increased in all AYA age groups during the most recent decades, but there were little clinical and epidemiological data from developing countries. There are 7,20,06,601(44.2%) people in Bangladesh under this AYA age group (15-39 years). This study aimed to determine the five-year survival rate of AYA cancer patients.
Methods: The study was a prospective fixed cohort study. The study period was from 2016 to 2021.
Results: Of the total 593 patients, the male and female ratio was 1:1.01. After a follow-up of 5

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years, it was documented that 278(46.88%) patients dropped out from follow-up. Among the remaining patients, 185(31.19%) died, and 130(21.92%) were alive. The alive male was 52(40.00%), the female was 78(60.00%), and the ratio was M: F=1:1.5. Highest survival were in germ cell tumour at 80%
followed by gestational trophoblastic tumour 77.77%, lymphoma 73.68%, breast cancer 63.64%, ovarian malignancies 57.14%, testicular cancer 50.00% and skin cancer 50.00%. None had insurance coverage, and 92% were dependent on treatment costs.
Conclusion: Evidence-based guidelines for AYA have not been developed for evidence-based late effects screening and care guidelines for AYA cancer patients. The high death (31.19%) occurrence is dangerously alarming for Bangladesh as youth are the majority of the total population. So methods should be searched to reduce the AYA death occurrences.

Keywords: AYA cancer; survival rate; epidemiology; Bangladesh.

ABBREVIATIONS

CI : Confidence Interval;
CNS : Central Nervous System;
PNET : Primitive Neuro-Ectodermal Tumours;
MPNST : Malignant Peripheral Nerve Sheath Tumor;
STS : Soft Tissue Sarcoma;
CUP : Carcinoma Unknown Primary;

1. INTRODUCTION

"The discipline of adolescent and young adult oncology (AYAO) is an evolving field that has begun to be defined only within the last decade. The increasing focus in the previous 15 years on the outcomes, unique challenges of care and different biology of young adult cancers is beginning to stimulate interest in developing clinical programs specific to the care of AYAs. Cancer is regarded as a disease in older adults. Little is known and reported in the literature about the incidence and patterns of this disease in adolescents and young adults (AYAs). This population poised between children and adults has been called the lost tribe" [1].

"Adolescent and young adult (AYA) cancer patients, aged 15–39 years at primary cancer diagnosis, form a distinct, understudied and underserved group in cancer care" [2]. "Overall cancer mortality declined from 2008 through 2017 by 1% annually across age and sex groups except for women aged 30 to 39 years, among whom rates were stable because of a flattening of declines in female breast cancer" [3-5].

There is no study on AYA malignancies in adolescents and young adults in Bangladesh. There are limited studies and works of literature available from developed countries. Although small, the annual number of AYA cancers will constitute a significant burden. This diagnosis disrupts the expected development trajectories, including physical, psychological, social and life goals related to family and careers. For these reasons, cancer in AYA merits attention.

"Early detection of the disease by recognizing signs and symptoms that appeared first will benefit the patients with AYA tumours as the prognosis differs with the stage of the disease. Although cancer is the second leading cause of death in AYA (12% of death), it is still relatively uncommon" [6]. "The incidence of cancer is increasing. Fortunately, with modern aggressive multidisciplinary therapy in developed countries, five-year survival for this group with cancer exceed 75%" [7].

"Many cancers, including lymphoma, leukaemia, sarcomas, melanoma, GI stromal tumour, breast cancer and colon cancer; the epidemiology and cancer biology differ in AYA cancers compared with younger children and older adults" [8-10]. "Recent studies have found differences in outcomes for AYA cancers in certain cancers depending on whether they were treated on pediatric or adult protocols. Generating and delivering treatment care plans for the AYA population requires awareness and sensitivity to these issues. The recommendation of the AYAO is to provide education, training, and communication to improve cognition, prevention, access, and quality of care for AYAs" [11].

"A need to examine survival trends of individual cancers in older adolescents and young adults is prompted by overall survival trends that have indicated a lack of progress in survival improvement for AYAs compared with younger and older cancer patients. AYA males had a worse survival rate than females" [12,13].

"AYA patients with cancer aged 15 to 39 years have not shown the same improved survival as older or younger cohorts" [14,15]. "The age limit of this study was 15 to 39 years. Our objective was to study the descriptive epidemiology of cancers in the AYA age group at NICRH and to compare this with the available data in other countries' literature. There are 7,20,06,601(44.2%) people under this 15-39 age group" [16,17]. They are in a vital age group not only for their development but also for their country. This study aimed to find out the 5-year survival rate of AYA cancer.

2. MATERIAL AND METHODS

The study was observational. All histologically confirmed cancer patients aged 15-39 who enrolled for treatment in the medical oncology department at the National Institute of Cancer Research and Hospital (NICRH) from January 2016 to December 2016(12 months) were enrolled for this study. Of the 593 patients included in the study. Their follow up were taken over the phone or departmental follow-up registries up to October 2021. Five years are counted individually from the date of diagnosis. The purposive sampling technique collected the sample. Before the commencement of this study, the research protocol was approved by the respective authority (RRC & EC) of NICRH, Dhaka. Consent was taken with written documents. After five years of completion of their treatment, each patient was interviewed on telephone and arranged according to the patient's condition like alive, dead, or lost to follow up. The follow-up patients were arranged according to Batch classification at the five-year interval.

3. RESULTS AND DISCUSSION

A total of 593 patients were enrolled. Of them, male (M) 295(49.75%), female (F) 298 (50.25%) and M: F=1:1.01. At the end of the 5-year follow-up, it was documented that 278(46.88%) patients were untraceable whose 125(21.10%) patients had no contact number, including males 49(39.20%), females 76(60.80%) and 153(25.80%) including male 87(56.86%), female 66(43.14%) were out of contact due to switch off of their mobile number. Among the remaining patients, 185(58.73%) patients died, including male 101(54.60%), female 84(45.40%), and the number of alive patients was 130 (41.27%), including male, 52(40%) and female 78(60%). In the number of dead patients, the male-female ratio was 1.2:1. Ratio of male-female alive patients was 1:1.5.

Table 1 displays the demographic profile of AYA patients in NICRH. According to data, the highest percentage of patients were homemakers, almost 39.29% (233 cases), followed by 18.18% (112 cases). The next highest were respectively job (11.97%), farmer (9.95%), business (7.93%), labour or worker are occupied 7.60%. The rest of the cases had no occupations (4.38%). In the case of literacy, data showed that 32.4 % of people were illiterate, and the rest of the issues were literate at different stages. From the data, 51.43%, i.e., i.e. 305 patients were poor, 31.53%, i.e. 187 patients were below average socioeconomic class, and the rest of the 24(4.05%) patients were in a suitable category.

The number at risk and five-year relative survival estimates with 95% confidence intervals of adolescent and young adult (AYA) cancer patients aged 15–39 years at time of diagnosis in Bangladesh between 2016-2021 and presented by age, sex, cancer type and period of diagnosis.

Of total 96 patients, it was documented that second highest survival rate were in colon cancer 6(60%) followed by stomach cancer 2(20%), gall bladder cancer 1(10%) and pancreatic cancer 1(10%). Esophageal cancer, periampullary cancer, Liver cancer and rectal cancer had 5 year survival rate 0%.

Data shows that the survival rate in Germ cell and trophoblastic neoplasms of the gonads is 80%, followed by Germ cell and trophoblastic neoplasms of non-gonadal sites rate of 77.77%. In the lymphoma case, the survival rate was 73.68%, followed by breast cancer at 63.64%. The lowest three survival rates were ovarian cancer 57.14%, leukaemia 33.33%, and sarcoma 21.25%.

Table 1. Demographic profiles of AYA patients are given

Age Range	**15-39 years**
Sex	
Male	295(49.75%)
Female	298(50.25%)
Occupation	
Farmer	59(9.95%)
Housewife	233 (39.29%)
Business	47(7.93%)
Job	71(11.97%)
Labor/Worker	45 (7.60%)
Student	112 (18.18%
Unemployed	26(4.38%)
Education	
Illiterate	190(32.04%)
Primary (Class v)	191(32.21%)
SSC (Class 10)	125(21.08%)
HSC (Class 12)	47(7.93%)
Graduate	23(3.88%)
Masters	12(2.02%)
Madrasa (Islamic education)	5(0.84%)
Economic status	
Poor	305 (51.43%)
Below average	187(31.53%)
Good	24(4.05%)

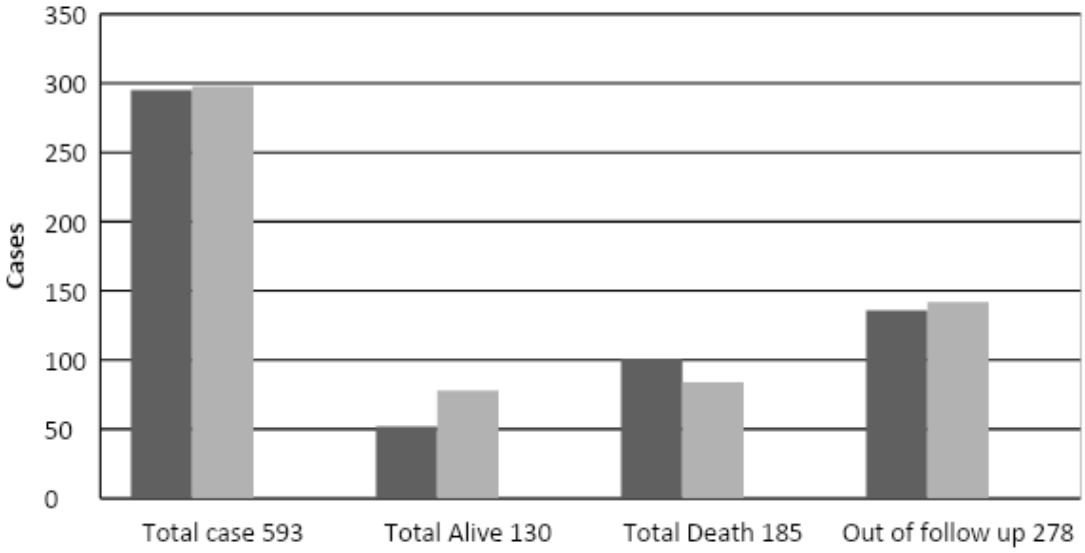

Fig. 1. Total cases with sex ratio including death and alive cases

Table 2. The number at risk and five-year relative survival estimates

Population Characteristics	Period of Diagnosis : 2016-2021	
	n at Risk	% RS (95% CI)
All cancers	593	41.27
Sex		
Male	295	33.99
Female	298	41.15
Cancer types		
Leukaemias	38	33.33
Acute lymphoid leukaemia	21	33.33
Acute myeloid leukaemia	9	40.00
Chronic myeloid leukaemia	8	50.00
Lymphomas	75	73.68
Non-Hodgkin lymphomas	39	66.66
Hodgkin lymphomas	36	68.42
CNS and other intracranial andintraspinal neoplasm		
Astrocytoma	9	33.33
Other gliomas	5	0.00
Ependymomas	1	0.00
Medulloblastomas and other PNET	1	0.00
Other specified intracranial andintraspinal neoplasms	1	100.00
Sarcoma (Osseous & STS)	122	21.25
Osteosarcomas	40	21.74
Chondrosarcomas	4	0.00
Ewing tumours	21	11.11
Fibromatous neoplasms	10	33.33
Rhabdomyosarcoma	3	0.00
Synovial sarcoma	8	33.33
Liposarcoma	3	33.33
Alveolar Sarcoma	2	0.00
MPNST	6	33.33
Embryonal Sarcoma	2	0.00
Myxosarcoma	3	33.33
Unspecified soft tissue sarcomas	23	21.74
Germ cell and Trophoblastic neoplasms	46	56.25
Germ cell and trophoblastic neoplasms of the gonads	39	80.00
Germ cell and trophoblastic neoplasms of non-gonadal sites	7	77.77
Melanoma and skin carcinomas	6	25.00
Melanoma	3	0.00
Skin carcinomas	3	50.00
Carcinomas	2	50.00
Thyroid carcinomas	21	40.00
Head and neck carcinomas	18	10.00
Carcinomas of lung	106	63.63
Carcinomas of breast	2	0.00
Carcinomas of kidney	2	0.00
Carcinomas of bladder	7	30.00
Carcinomas of gonads	16	25.00
Carcinomas of cervix	4	50.00
Carcinoma of uterus	17	57.14
Carcinomas of ovary	5	0.00

Population Characteristics	Period of Diagnosis : 2016-2021	
	n at Risk	% RS (95% CI)
Carcinoma esophagus	44	20.69
Carcinomas of colon & rectum	23	7.70
Carcinomas of the stomach	3	0.00
Carcinomas of liver	6	0.00
Carcinoma bile ducts	6	33.33
Carcinomas of pancreas	2	0.00
Periampullary carcinoma	2	50.00
Testicular carcinoma	2	50.00
CUP	5	33.33

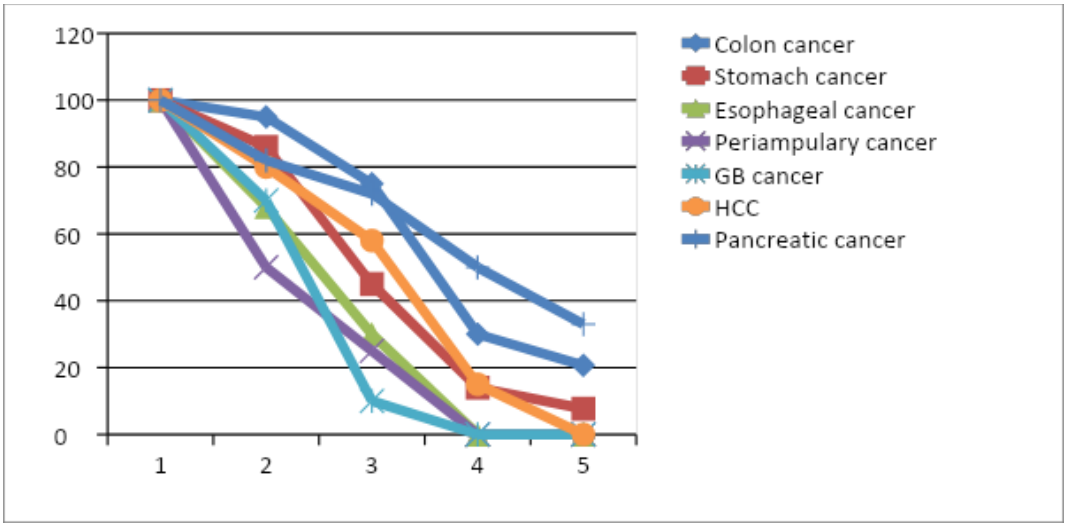

Fig. 2. 5 years survival rate from GIT cancer in AYA patients

Fig. 3 shows that about 33% economically superior patients, 19.67% poor and 18.18% average economical patients survived five years.

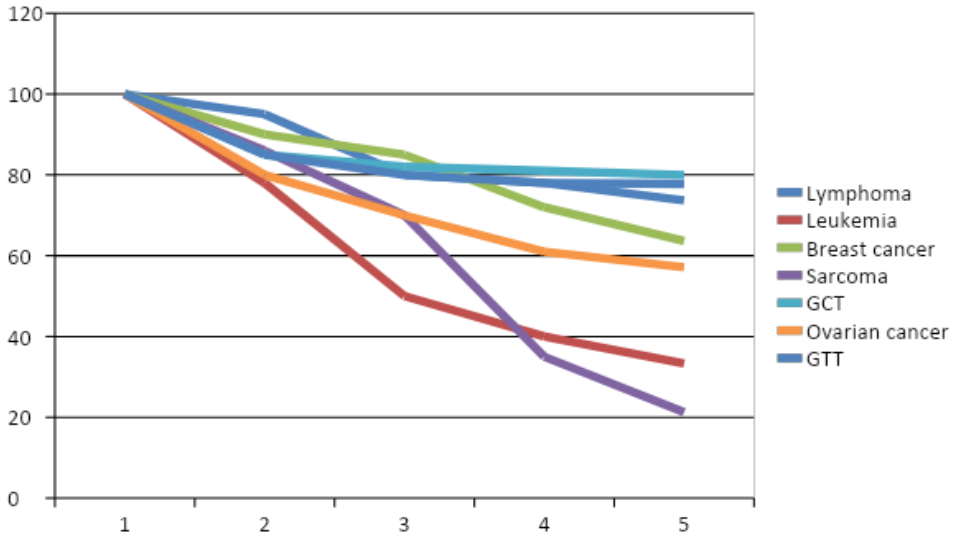

Fig. 3. 5 years survival rate according to economical status

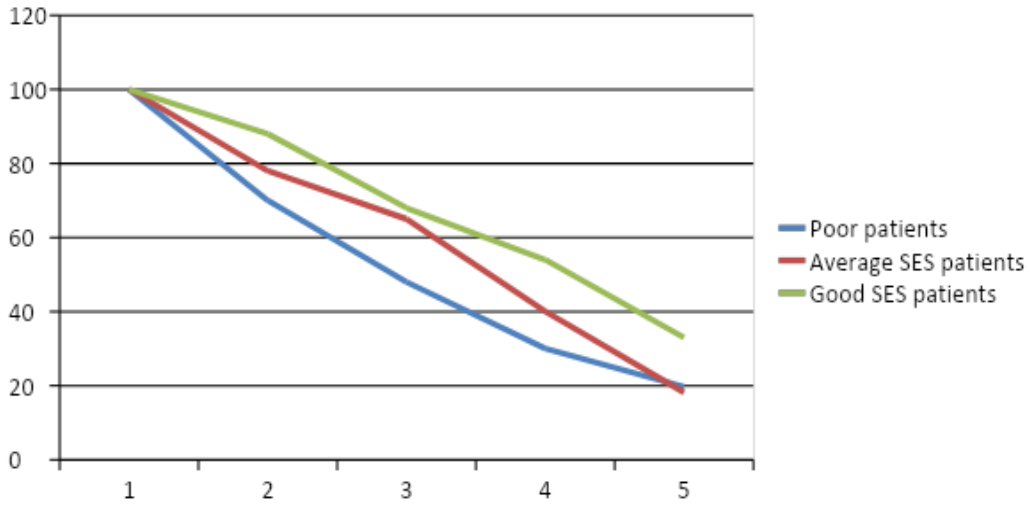

Fig. 4. Five years survival rate according to economical status

It was documented that delay in starting treatment from diagnosis impacts survival. Patients were categorized according to delay to start treatment and showed five-year survival was 18.18%, 17.4%, 16.66%, 12.5% and 10.42% of patients who made delayed starting treatment for one month, two months, three months, 4-6 months and more than six months respectively.

It was observed that the highest survival rate of 40% was in patients who are tobacco non users and without comorbidities. The 5-year survival rate in smokers was 14.47%, and 15% in smokeless tobacco users. The lowest (5-year OS 0%) survival rate was observed in those patients with comorbidities.

35% of AYA patients were from rural and urban dwellings, respectively. On the other hand, the five-year survival rate was high in urban patients, about 27%, whereas in rural patients, survival was only 21.66%.

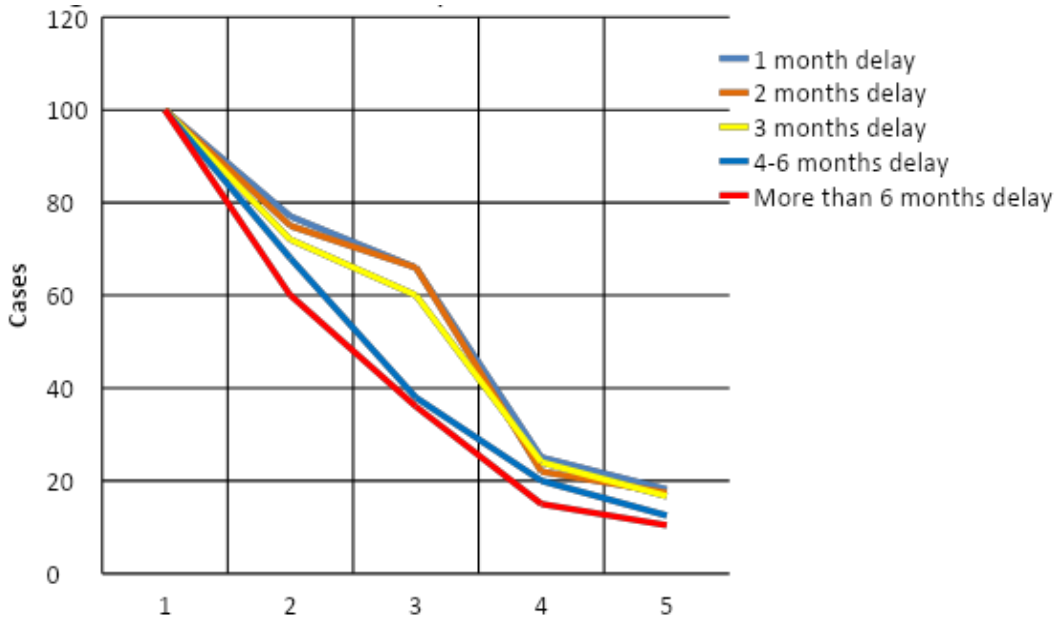

Fig. 5. Treatment delay and outcome

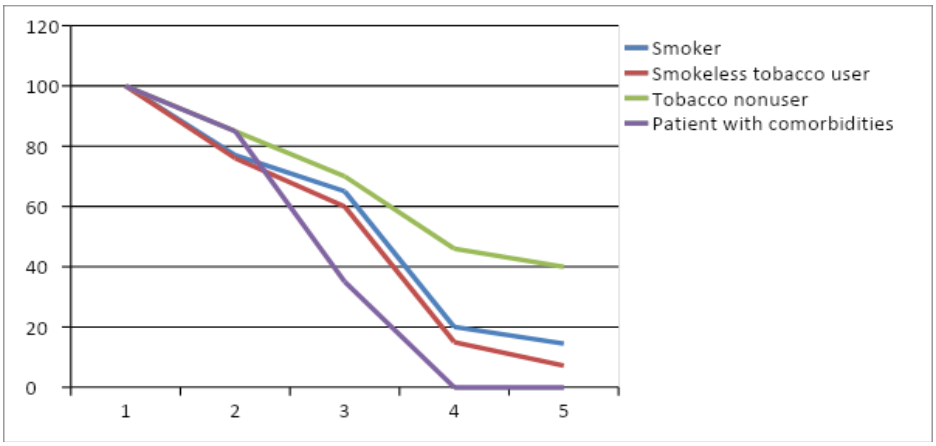

Fig. 6. Five year survival rate according to personal habit/comorbidities

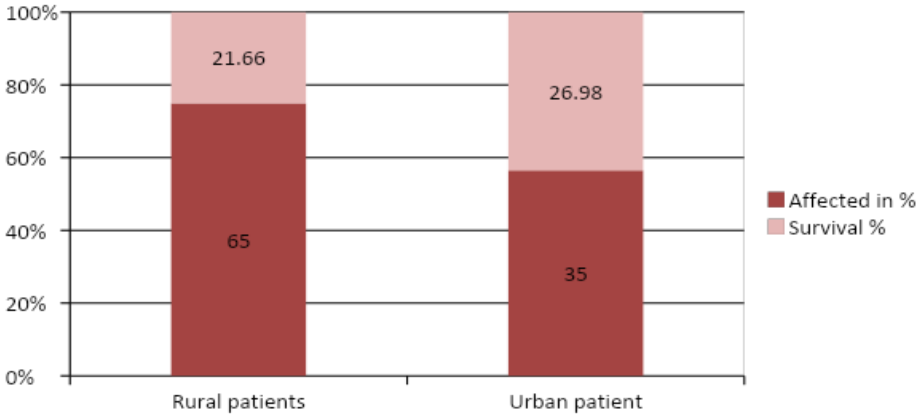

Fig 7. Incidence and 5 years survival rate according to residence

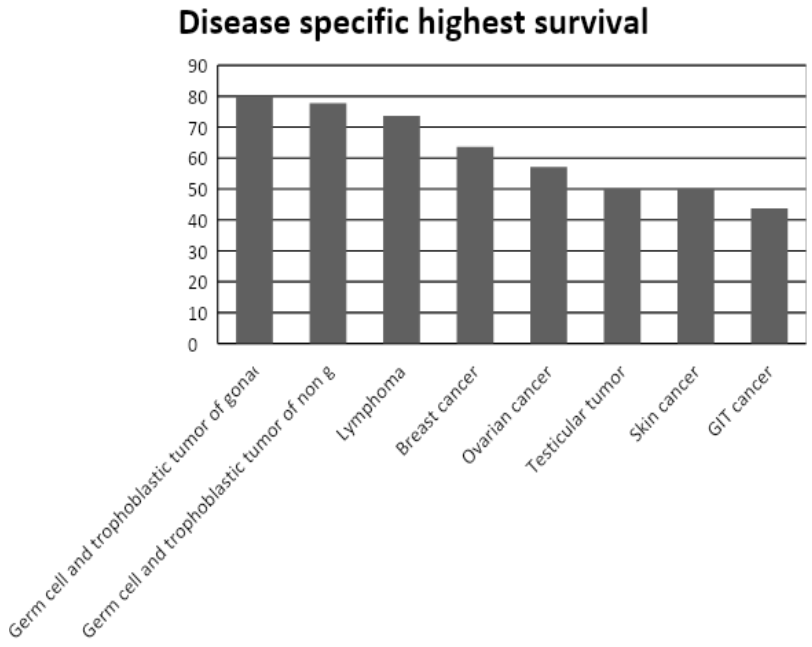

Fig. 8. Disease specific highest alive in percentage

Fig. 8 showed the highest survival rate in Germ cell and trophoblastic neoplasms of the gonads, which was 80%, followed by germ cell and trophoblastic neoplasms of non-gonadal sites survival rate of 77.77%. In lymphoma, the survival rate was 73.68%, followed by breast cancer at 63.64%, ovarian cancer at 57.14%, testicular cancer at 50.00%, skin cancer at 50.00%, and GIT cancer survival rate was 43.75%.

4. DISCUSSION

This study provided a comprehensive overview of 5 years long-term trends in survival and mortality among AYA cancer patients aged 15–39 years in Bangladesh from 2016 through 2021. Our findings further highlight a changing pattern in the distribution of cancer types based on AYA sex, age, residence, personal habits, treatment period, economic status and impact on treatment outcome due to delay of starting therapy from diagnosis.

“Over time, the spectrum of cancers in AYA is distinct and differs considerably from that in pediatric and older adult cancer patients” [18-21]. Our data will add to this and present the distribution of AYA cancers over time and several other factors, highlighting the data from 2016-2021. Our findings emphasize the importance of distinguishing the data based on sex, cancer types, residence, economic status, personal habits, and delay in starting the treatment and diagnosis. Based on these different factors, the AYA cancers differ substantially over the years.

The reasons for the shortage of survival improvement duration from the disease, is tobacco smoking [22-24]. The most critical factors are lack of awareness of the cancer problem in the specific age group, lack of health insurance coverage, follow-up gap and access to healthcare services. Another problem is the lack of clinical and translational research on cancer for AYAs and the dedicated health services to cancer patients. According to our data, male AYA cancer patients have a worse survival rate than females, which can be due to different psychological factors such as higher risk-taking behaviour, personal habit and lower adherence to treatment [25-26].

In line with previous global findings, rising trends in incidence were among the highest for AYAs diagnosed with thyroid and kidney carcinomas, and a markedly higher burden of thyroid carcinomas was observed within the female AYA population [27,28]. The highest survival rate in Germ cell and trophoblastic neoplasms of the gonads is 80%, followed by Germ cell and trophoblastic neoplasms of non-gonadal sites at 77.77%, lymphoma at 73.68%, breast cancer at 63.64%. The lowest three survival rates were ovarian cancer (57.14%), leukaemia (33.33%), and sarcoma (21.25%). The highest death rate was observed in lung cancer(61%), followed by head neck cancer(57%), Sarcoma (46%), GIT Cancer (40.63%) and leukaemia (35%).

The residence of the patients has a significant impact on the survival rate. Fig. 7 shows that the residents of the urban area have more survival rate(26.98%) than in rural areas (21.66%). Our findings could ensure that it happened due to a lack of awareness of cancer, negligence towards the disease and treatment facilities better in urban than rural areas. The literacy rate of rural people was less than urban people. Therefore, their knowledge about disease and treatment and awareness is less than those who are aware of cancer. Different types of awareness programs are held in the urban area; that’s why urban people are more familiar. Nowadays, various organizations arrange online awareness programs, which can substantially change circumstances. Hopefully, this discrimination between rural and urban areas will change a few years later.

In the case of economic status, our findings showed that (Fig. 4) poor patients (18.18%) relatively have a 5-year survival rate than good (33%) and average (19.67%) social and economic status. Since cancer treatment is expensive in Bangladesh, poor and average social-economic status patients cannot afford the treatment cost. Patients who delay starting treatment from diagnosis have an impact on survival rate, which is related to their economic status. Poor patients delay starting their therapy from diagnosis. The difference between a 1-month (18.18%) and six months (10.42%) delay was 7.76%. Our findings conclude that if patients start their treatment soon after the diagnosis, the survival rate might be higher than the delayed treatment.

Patients with several personal habits could change their survival rate. Tobacco non-user has the highest percentage (40%) survival rate in 5 years patients with comorbidities have less survival.

Promising declines in AYA cancer mortality have been observed since the 1970s. Although not directly stated, more noticeable decreases for most specific cancer types among female AYAs were also observed by Close and colleagues [29-31]. Our analyses showed that different factors affecting the survival rate include personal habits, residence and economic status. A recent study with SEER data between 2008–2017 showed a similar 1% average decline per year for both sexes, whereas it levelled off for women aged 30–39 years, likely reflecting stabilizing breast cancer mortality trends [32]. Another recent American study (2020) on time-related long-term mortality trends among five-year AYA cancer survivors showed no disparities between sexes at 5, 10 and 20 years of follow-up [33]. However, their analyses did show marked improvements in late all-cause mortality that were mainly driven by temporal decreases in the mortality of primary cancers. Still, time-related improvements were less consistent across cancer types. As suggested, these findings likely reflect advances in cancer therapies and refinement of treatment strategies and might help identify priority groups for long-term surveillance to reduce late mortality from cancer. Continuing monitoring of (long-term) mortality trends among AYAs is therefore essential.

Finally, it could be that the trends observed in this study are the results of using the entire AYA age range and all stages combined. In contrast, some trends might only become apparent with more narrow age groups and individual disease stages.

5. CONCLUSION

In AYA, the death occurrences were 170(35.94%) and tract out of follow-up were 170(28.67%). This high death occurrence is dangerously alarming for developing countries as youth are the majority of the total population in developing countries. So methods should be searched to reduce the AYA death occurrences. AYA cancer patients vary among different countries across the world. More research in this field will help us understand the needs of Bangladesh's special young reproductive population. Cancer in AYA is a critical problem that has gone unrecognized or was only a peripheral concern among numerous research, medical and health services payer, patient support and advocacy, funding, and cancer surveillance constituencies, as well as healthy teenagers and young adults who do not know they are at risk for cancer. Progress in reducing cancer morbidity and mortality among AYAs could be addressed through more equitable access to health care, increasing clinical trial enrollment, expanding research and greater alertness among clinicians and patients for early symptoms and signs of cancer. Further progress could be accelerated with increased disaggregation by age in research on surveillance, aetiology, basic biology, and survivorship.

6. RECOMMANDATION

Following recommendations can be given based on this study:

1. Provide education, training and communication to improve awareness, prevention, access, and quality of care for AYA cancer.
2. Identify age related warning clinical features.
3. Ensure excellence in service delivery regarding prevention, screening, diagnosis, treatment, survivorship and end of life.
4. Identify the characteristics that distinguish the unique cancer burden in the AYAO patient.
5. Support the AYA cancer patient.
6. Health insurance.

CONSENT

As per international standard or university standard, Participants' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study design was approved by the ethical committee of Department of Medical Oncology, Shaheed Suhrawardy Medical College Hospital before implementation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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