

Adolescent and Young Adult Cancer

Adolescent and Young Adults with Gastric Cancer (AYA-GC)—The Dilemma of an Under-Represented Group: A Multi-Institutional Analysis from the Indian Subcontinent

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Keywords

- ▶ adolescent and young adults
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- ▶ incidence
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- ▶ Network of Oncology Clinical Trials in India

Gastric cancer (GC) is often ignored at a young age, which frequently leads to tragic consequences. The worldwide incidence of GC is increasing at a young age. In view of the limited Indian publication, we sought to characterize clinicopathological parameters and risk factors in the adolescents and young adults (AYA) population. Retrospective data from six centers (which are part of the Network of Oncology Clinical Trials in India) from 2015 to 2020 were collected from patient (18–39 years of age) records. This study was approved by the institutional ethical committee of individual centers. All statistical analyses were performed using Microsoft Excel and SPSS (Version 20). Data interpretation along with the analysis of obtained results was carried out using the following tests: Qualitative data was expressed in terms of frequency/percentage. One-hundred fifty-two AYA GC patients were enrolled. The 31 to 39 years age group was most affected in which 76.3% were females. The majority of patients were nonalcoholic (93.4%), nonsmokers (98.0%), and without a family history (98.0%). The most common (MC) presenting symptom was abdominal pain (67.1%). MC site was antrum (48%). Among esophagogastric junction cancers, the majority were type I and II Siewert

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classifications (77% [20/26] patients in cardia), MC histology—signet ring cell (67.1%) followed by diffuse-type (65.1%). Most were poorly differentiated (65.1%) and were diagnosed at an advanced stage (III & IV= 54.6%). This is one of our country's first large multicenter studies on GC in the AYA population. There was a higher female prevalence, aggressive tumor behavior and the majority of patients were diagnosed at a more advanced stage. The majority were nonsmokers with a negative family history. Awareness among general people, researchers, clinicians, and policymakers must be improved to better the loss of life years in the younger population.

Introduction

Ranked as the leading cause of mortality globally,¹ gastric cancer (GC) was previously deemed to be a malignancy limited to the elderly age group, occurring most commonly at an average age of 68 years in the United States with more than 95% of these patients aged 40 years² and above. Henceforth, majority of the study or clinical trials tend to focus on this group of patients with evidence-based approaches and management guidelines for them. It is imperative to note that the adolescent and young adults (AYA) population globally delivers to a nation's economy and is required to contribute to various healthcare-related taxation laws yet are devoid in terms of definite approach and tailored treatment of various malignancies such as GC due to its low incidence in this age group. The patients in the AYA-GC tend to present at an advanced stage carrying a poorer prognosis as compared to the elderly population with lowered life expectancy.^{3,4} In a recent study based on the Chinese population with GC, the prime focus was on the tendency of GC and its dissimilarity to the GC in the geriatric population.⁵ It is an unmet need of the hour for a country like ours to identify the AYA-GC group that is often under-represented due to low awareness not only among patients and respondents but also the healthcare practitioners, leading to a delayed time to diagnosis and treatment thereby compromising the outcome and life expectancy of the patient and affecting disease affected life years. There are few papers from our country that highlight the low survival and advanced stage of presentation in this age group.^{6,7}

Methods

A review of the literature was performed by downloading research articles from PubMed Central, with keywords such as young GC characteristics, GC in adolescents, and GC in young adults. Retrospective data of 152 patients (18–39 years) admitted between the years 2015 to 2020 were collected from multiple institutes across India that are part of the Network of Oncology Clinical trials India (NOCI): Registry of Cancers (www.noci-india.com). This study was approved by the institutional review board of all individual centers and the patient's consent was taken. All these patients were followed up by dint of outpatient department sojourns or telephonically. Data on clinical features, laboratory, and pathology were collected from the medical records of each

patient available in the medical archives of six hospitals. The data was anonymized and entered into a common database. All statistical analyses were performed using Microsoft Excel and SPSS (Version 20). Data interpretation along with the analysis of obtained results was carried out using the following tests: Qualitative Data was expressed in terms of frequency/percentage.

Results

Baseline characteristics have been summarized in [Table 1](#). A total of 152 patients' data was available for analysis; it was observed that the majority of the patients were affected in the age group of 31 to 39 years and of these (median age: 35 years), 116 (76.3%) were female. In terms of substance abuse history, it was observed that of the 152 patients, a history of alcohol consumption was present in 10 patients (6.6%) and the remaining 142/152 (93.4%) had no history of alcohol abuse; only 3/152 patients (2.0%) had a history of tobacco usage (in any form), whereas majority comprised of the nonsmoker population 149/152 (98%).

The most common presenting complaint was that of abdominal pain 102/152 (67.1%) with associated loss of weight, appetite, and other symptoms in 50/152 (32.9%) patients. It was observed that the majority of patients had the primary lesion located in the antrum of the stomach 73/152 (48%) followed by the body (53/152; 34.9%) and cardia (26/152; 17.1%); type I and type II esophagogastric junction (20/152) Siewert classifications were equal (10 each; 38.5%) and the remaining 6 (23.1%) belonged to type III. In terms of pathology, as per World Health Organization (WHO) classification, the majority consisted of the SRH (signet ring histology) (102/152; 67.1%) followed by mucinous histology (36/152; 23.7%). Based on Lauren's classification, the diffuse variant was more prevalent (99/152; 65.1%). Most were poorly differentiated (65.1%). The majority were diagnosed at an advanced stage (III and IV= 54.6%).

Discussion

Gastric adenocarcinoma was thought to be a disease of the elderly and the geriatric population with only 1/10th of these in patients below the age of 45 years.⁸ This study was an attempt to address this issue from the Indian subcontinent thereby breaking the ice to open a road to better treatment options and screening programs and better recognition by

Table 1 Clinicopathological characteristics and risk factors

| Clinicopathological characteristics and risk factors | n = 152 | % |
|-------------------------------------------------------------------------------------|---------|------|
| Age at diagnosis | | |
| <20 | 0 | 0.0 |
| 20–30 | 30 | 19.7 |
| 31–39 | 122 | 80.3 |
| Gender | | |
| Male | 36 | 23.7 |
| Female | 116 | 76.3 |
| Alcoholic | | |
| Yes | 10 | 6.6 |
| No | 142 | 93.4 |
| Smoker | | |
| Yes | 3 | 2.0 |
| No | 149 | 98.0 |
| Family history | | |
| Yes | 3 | 2.0 |
| No | 149 | 98.0 |
| Presenting complaints | | |
| Abdominal pain | 102 | 67.1 |
| Others | 50 | 32.9 |
| Site of the primary disease | | |
| Cardia | 26 | 17.1 |
| Body | 53 | 34.9 |
| Antrum | 73 | 48.0 |
| Siewert classification for cardia with gastroesophageal junction involvement | | |
| Type I | 10 | 38.5 |
| Type II | 10 | 38.5 |
| Type III | 6 | 23.1 |
| Histopathology (WHO) | | |
| Papillary | 7 | 4.6 |
| Tubular | 7 | 4.6 |
| Mucinous | 36 | 23.7 |
| Signet ring cell | 102 | 67.1 |
| Mixed | 0 | 0.0 |
| Histopathology (Lauren) | | |
| Intestinal | 40 | 26.3 |
| Diffuse | 99 | 65.1 |
| Indeterminate | 13 | 8.6 |
| Grade | | |
| Well differentiated | 23 | 15.1 |
| Moderately differentiated | 30 | 19.7 |
| Poorly differentiated | 99 | 65.1 |

Table 1 (Continued)

| Clinicopathological characteristics and risk factors | n = 152 | % |
|------------------------------------------------------|---------|------|
| TNM staging | | |
| I | 13 | 8.6 |
| II | 46 | 30.3 |
| III | 50 | 32.9 |
| IV | 33 | 21.7 |
| Missing data | 10 | 6.6 |

Abbreviations: TNM, tumor, node, metastasis; WHO, World Health Organization.

policyholders, healthcare workers, and those involved in providing cancer care. A recent study from 2019 by Zhao et al observed that the mean age of presentation is 35.6 to 40.5 years with female preponderance with the majority of tumors situated in the distal stomach with advanced disease at the time of presentation that is in direct concordance with our study.⁹

In comparison to other AYA-GC data published by Lee et al,¹⁰ we observed that all findings related to the age group of presentation, sex predilection, and advanced stage at presentation were in concordance; however, the Korean study comprised of patients of approximately 32% being smokers and 20% with a family history, whereas our study had a prevalence of nonsmokers and a negative family history in 98% of the patient population, suggesting thereby a more sporadic and aggressive variant in the Indian subcontinent.

Furthermore, it has been already published that the age more than 70 years is an independent poor prognostic factor in this group.¹¹ However, in comparison to this group of patients,^{12,13} we observed that in elderly patients, presentation in the form of upper gastrointestinal bleeds (such as black tarry stools, hematemesis, and anemia) tends to be more common as opposed to the resentation of abdominal pain in the AYA population. We also observed that relatively higher prevalence of gastric adenocarcinoma in men (72%) with a history of smoking (35–42%), moderately differentiated (poorly differentiated in AYA) and SRH being highly uncommon. Whereas SRH was found to be more common in our group of patients (67.1%).

Henceforth, it is evident from our study that AYA-GC group is under-represented and goes unacknowledged leading to a delay in diagnosis and treatment, thereby compromising the outcome in an already aggressive primary with a poor histology-associated disease process leading to untimely deaths and reduced overall survival. The mortality figures from Indian registries suffer from the problem of under-reporting because of problems in the registration of death and in reporting of cause of death.¹⁴ Similar challenges were faced in our retrospective data collection, and it stresses the importance of maintaining a prospective database. Our network cancer registry

software is now functional, and this collaborative effort shall help us in reporting authentic treatment outcomes in the future.

Conclusion

This is one of our country's first large multicenter studies on GC in the AYA population. There was a higher female prevalence, aggressive tumor behavior, and the majority of patients were diagnosed at a more advanced stage. The majority of the patients neither have a family history nor a smoking history. Awareness among general people, researchers, clinicians, and policymakers must be improved to better the loss of life years in the younger population.

Clinical Trials Registry-India (CTRI) Number: CTRI/2022/01/039233

Ethical Approval

The study was approved by the Institutional Ethics Committee (vide IMS.SH/SOA/2021/097 letter dated 07.07.2021). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

None declared.

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