Reliance on Self-Medication Increase Delays in Diagnosis and Management of GI Cancers: Results From Nepal

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PURPOSE
Patients with GI cancers in Nepal often present with advanced disease and poor outcomes. The purpose of the study was to determine the time to presentation, diagnosis, and treatment of GI cancer and the baseline factors that may be associated with delays.

PATIENTS AND METHODS
An institutional review board–approved study was performed in Kathmandu, Nepal, from July 2018 to June 2019. Patients with newly diagnosed GI cancers were asked to fill out a standardized questionnaire. Baseline factors such as residence, literacy, and use of self-medication were recorded. Patients were asked to report the time from first symptom to presentation, time from primary care visit to pathologic diagnosis, and time from diagnosis to surgery and/or treatment. Baseline factors were analyzed using 2-tailed t tests (Prism 8.0; GraphPad, La Jolla, CA) to determine whether any factors were associated with longer time delays in these 3 intervals.

RESULTS
The cohort comprised of 104 patients with a median age of 53.5 years (range, 22-77 years); 61.5% were men, 46.2% had upper GI cancers, and 83.7% presented with stage III or IV disease. The median time to presentation was 150 days, time to diagnosis was 220 days, and time to treatment was 50 days. There was no statistically significant difference in time intervals between upper and lower GI cancers. Use of self-medication (88.5%) was the only factor associated with longer time intervals to presentation, diagnosis, and treatment.

CONCLUSION
Patients in Nepal have long time intervals to presentation, diagnosis, and treatment of GI cancer. Self-medication led to longer delays. Reasons for self-medication and other potential barriers will be explored in future studies in the hopes of improving outcomes.

INTRODUCTION
GI cancer represents a major health challenge worldwide including in Nepal, where patients often present with advanced disease and outcomes are poor. In Nepal, stomach cancer ranks as the fifth most common cancer (5.9% of 26,184 new cancers in 2018), and colon and rectal cancer rank 10th (2.6%) and 11th (2.5%), respectively.1 Therefore, GI cancers in total place a significant burden on the health care system in Nepal.

A key factor to improve cancer outcomes is to detect and treat cancers as early as possible. Nepal has many barriers to early detection including a lack of awareness about the risk factors, symptoms, and prognosis of cancer among patients, their family, and even health care professionals. Patient delays may occur when the patient fails to recognize and act on suspicious cancer symptoms. This may be especially true in GI cancers because there are often no unique symptoms, and early symptoms are often treated by the patients with medications such as those for acid peptic disease.2 The practice of self-medication among patients with cancer appears to be common in Nepal.

Health care professionals who do not recognize symptoms as serious, limited access to health services, and delays in investigations and referrals can lead to primary care delays. Secondary care delays may occur when a patient with a suspected cancer is not seen on time, when there are further delays in investigations, or when the patient is referred to the wrong specialty.3 These barriers are further augmented by the lower socioeconomic status of many patients, the high percentage of rural patients, the complex geographical terrain and distance from health care facilities, and other factors embedded in the social and cultural
context in Nepal. All of these factors may contribute to a delay in presentation of patients to the hospital, increasing the number of patients diagnosed with advanced-stage cancers.

Thus, the purpose of this study was to quantify the time from first symptoms to diagnosis and treatment of patients with upper GI (UGI) or lower GI (LGI) cancer in Nepal. We sought to explore baseline factors that may contribute to delays in care such as self-medication, geographic location, and literacy. The overall goal is to use this information to help guide infrastructure changes and educational initiatives to improve the time to presentation, diagnosis, and treatment and hopefully outcomes in Nepalese patients with GI cancers.

PATIENTS AND METHODS

This was a cross-sectional study conducted at the Department of Clinical Oncology, National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal. Approval was obtained from the institutional review board of the National Academy of Medical Sciences, Bir Hospital. Written informed consent was obtained from each patient diagnosed with GI cancer (esophageal, gastric, small intestinal, colon, rectal, or anal cancer).

All newly diagnosed consenting patients with GI cancers, both in- and outpatients, were enrolled from July 2018 to June 2019. Patients were asked to fill out a standardized questionnaire (Data Supplement). Caregivers were allowed to answer on behalf of illiterate patients. Information collected included patient demographics such as age, sex, address, occupation, and education, as well as cancer-specific information such as presenting symptoms, duration of symptoms, interval from first symptom to diagnosis and treatment, and history of self-medication.

Regarding self-medication, some patients used multiple self-medications, but we reported the drug that was used predominantly as self-medication. Patients were also asked about their understanding of their site and stage of cancer, as well as their understanding about smoking and alcohol risk factors and the importance of family history. Review of medical records was also done to extract patient clinico-pathologic information.

The following three time intervals were recorded: time to patient presentation, which was defined as time from first symptom to first medical consultation; time to diagnosis, which was defined as the time from primary care referral to cytologic or pathologic diagnosis; and time to treatment, which was defined as the time from diagnosis to surgery and/or treatment by a medical or radiation oncologist.

Data Collection and Statistical Analysis

Frequencies and percentages were obtained for each categorical variable. The mean and median were obtained for continuous variables. SPSS, version 24, statistical software (SPSS, Chicago, IL) was used for statistical analyses. The nonparametric Mann-Whitney U test was used to compare the median time intervals between UGI and LGI cancers. Differences in median times intervals were compared using 2-tailed t tests (Prism 8.0; GraphPad, La Jolla, CA) based on the identified potential causes of delays. A 2-tailed level of significance of P < .05 was considered significant and was applied to all statistical tests.

RESULTS

During the study period, 111 patients met eligibility criteria, with 104 patients (94%) consenting and completing the questionnaire. Baseline demographic and clinical characteristics of the patients are listed in Table 1. The median age at diagnosis was 53.5 years (range, 22-77 years), and 61.5% of patients were men. Rural patients made up 74% of the cohort, and at diagnosis, 76 patients (73%) were outpatients. In terms of level of education, 68.3% of patients were illiterate. Regarding occupation, 46.2% were farmers, whereas 28.8% were housewives. Seventy-nine percent of patients were unaware of risk factors (specifically smoking, alcohol, and family history) associated with GI cancers.
cancers. The majority of patients (68.3%) had a history of smoking, including 77.1% with UGI cancers and 60.7% with LGI cancers. In total, 46.2% of patients consumed alcohol, 56.3% with UGI cancers and 37.5% with LGI cancers.

Colorectal cancer was seen in 54% of patients (left-sided colon, 23%; right-sided colon, 13%; rectum, 18%), and 46.2% had gastroesophageal cancer (gastric, 38.5%; esophagus, 7.7%). Stage III or IV disease at diagnosis was found in 83.7% of patients (87.5% in esophageal cancer, 90% in stomach cancer, 67.5% in colon cancer, and 100% in rectal cancer). No patients with anal or small bowel cancer were identified.

For patients with UGI cancers, abdominal pain and weight loss were the most commonly reported symptoms, as shown in Table 2. For those with LGI cancers, weight loss, bleeding per rectum, and abdominal fullness were the most common symptoms. Most patients (88.5%) had a history of self-medication before their first medical consultation. These medications are listed in Table 3. Alternative medicines were used in 52.8% of patients, followed by antacids in 23.1%. Alternative medicines included a variety of compounds, including traditional spices or herbs, multivitamins or enzymes, honey, lemon, and black pepper, or medicines prescribed by ayurvedic doctors or traditional healers.

The time intervals to presentation, diagnosis, and treatment of patients are listed in Table 4. In the entire cohort, the median time to patient presentation was 150 days (range, 15-730 days), median time to diagnosis was 220 days (range, 29-1,125 days), and median time to treatment was 50 days (range, 15-90 days). When these time intervals were broken down by UGI and LGI cancers, there was no statistically significant difference in the time to presentation (150 vs 143 days, respectively; \( P = .62 \)), time to diagnosis (217 vs 220 days, respectively; \( P = .59 \)), or time to treatment (58 vs 45 days, respectively; \( P = .06 \)).

The association between each time interval and baseline variables is detailed in Table 5. The only identified baseline variable that consistently influenced all three time intervals in a statistically significant way was self-medication. Geographic location, literacy status, and awareness of risk factors were not associated with the time to presentation, diagnosis, or treatment.

### Table 1. Baseline Demographic and Clinical Characteristics of the Study Population

| Characteristic | No. of Patients (%) |
|----------------|---------------------|
| Median age, years (range) | 53.5 (22-77) |
| Male sex | 64 (61.5) |
| Residence | |
| Rural | 77 (74) |
| Urban | 27 (26) |
| Education | |
| Literate | 33 (31.7) |
| Illiterate | 71 (68.3) |
| Occupation | |
| Farmer | 48 (46.2) |
| Housewife | 30 (28.8) |
| Service | 8 (7.7) |
| Other | 18 (17.3) |
| Smoker | 71 (68.3) |
| Alcohol consumer | 48 (46.2) |
| Site of disease | |
| Esophagus | 8 (7.7) |
| Gastric | 40 (38.5) |
| Colon | 37 (35.6) |
| Rectum | 19 (18.3) |
| Small intestine/anal canal | 0 (0) |
| Stage of disease | |
| I | 0 (0) |
| II | 17 (16.3) |
| III | 66 (62.5) |
| IV | 22 (21.2) |
| Prior awareness of risk factors of GI cancer | 22 (21.2) |
| Use of self-medication | 92 (88.5) |

*Values are numbers and percentages, unless otherwise noted.

### Table 2. Presenting Symptoms

| Symptom | Upper GI Cancer | Lower GI Cancer | \( P \) |
|---------|-----------------|----------------|-------|
| Abdominal pain | 40 (83.3) | 18 (32.1) | < .00001 |
| Weight loss | 33 (68.7) | 34 (60.7) | .42 |
| Vomiting | 28 (58.3) | 17 (30.3) | .006 |
| Hematemesis | 25 (52.1) | 0 (0) | < .00001 |
| Melena | 25 (52.1) | 0 (0) | < .00001 |
| Decreased appetite | 21 (43.7) | 30 (53.5) | .33 |
| Abdomen fullness | 20 (41.6) | 31 (55.3) | .18 |
| Dysphagia | 14 (29.1) | 0 (0) | < .00001 |
| Altered bowel habit | 2 (4.1) | 27 (48.2) | < .00001 |
| Per rectal bleeding | 0 (0) | 33 (58.9) | < .00001 |

### Table 3. Types of Self-Medication

| Medication | Upper GI Cancer | Lower GI Cancer | Total | \( P \) |
|------------|-----------------|-----------------|-------|-------|
| Alternative medicines | 26 (54.1) | 29 (51.7) | 55 (52.8) | .85 |
| Antacids | 12 (25) | 12 (25) | 24 (23.1) | .82 |
| Analgesics | 3 (6.2) | 7 (12.5) | 10 (9.6) | .33 |
| Prokinetics | 2 (4.1) | 1 (1.7) | 3 (2.8) | .59 |

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DISCUSSION

Prolonged time intervals in presentation, diagnosis, and treatment can be a challenge for many patients with cancer but are especially challenging in developing countries, where there are greater challenges and barriers to the access and use of health services. In our study, the median time interval to patient presentation was 150 days, median time to diagnosis was 220 days, and median time to treatment was 50 days. There was no statistically significant difference in the time intervals between UGI and LGI cancers. There are no universally accepted benchmarks for these time intervals for most cancers; however, when compared with other published literature from Western countries, Nepalese time intervals are longer.7,8 In one published study from India, the mean time from symptoms to cancer diagnosis ranged from 15 days to 3 years and varied greatly depending on whether patients presented with their symptoms to a large government hospital or outside that hospital. Use of an alternative medication was also identified as a factor causing delayed presentation.9

Most patients presented with advanced-stage disease (stage III or IV), which affects treatment and outcomes. There are many possible reasons for this, but the prolonged time intervals are an important component.

We hypothesized that patients from rural areas (74% of patients) would have greater time delays given that Nepal has significant geographic barriers with its difficult terrain and distances to health care centers and the fact that many people must walk to health care centers.10 A few studies have compared multiple time intervals to treatment of rural and urban patients and reported that rural patients with colorectal cancer had a longer time from presentation to diagnosis and treatment.11,12 However, we did not find that in our study. We thought being illiterate might be associated with greater time delays, but this was not seen. We also hypothesized that patients who were aware of GI cancer risk factors would have shorter time delays, but this was not found in our study.

The only baseline factor associated with greater delays in the presentation, diagnosis, and treatment of cancer was the use of self-medication, which was practiced by 88.5% of our patients. This is comparable to data from India, where 87% of patients with cancer took self-medication for various reasons.13 A wide variety of alternative medicines were used in more than half of our patients, followed by antacids in almost one quarter of patients. The use of complementary and alternative medicine is common in Nepal for many diseases.14 The empirical use of antacids has also been widely practiced in other parts of the world and shown to delay diagnosis.15 It is unknown from our study whether the use of self-medication is a result of difficulty seeking medical attention because of cost and/or distance, reluctance to seek medical attention because of distrust or cultural factors, or the belief that the symptoms are nothing serious or that the medication will actually help. We plan to explore the reasons for self-medication use further to find factors that are amenable to change. For example, health services utilization

| Time Interval | Total Median Time (days; range) | Median Time for Upper GI Cancer (days) | Median Time for Lower GI Cancer (days) | P |
|---------------|---------------------------------|--------------------------------------|--------------------------------------|----|
| Time to patient presentation | 150 (15-730) | 150 | 143 | .62 |
| Time to diagnosis | 220 (29-1,125) | 217 | 220 | .59 |
| Time to treatment | 50 (15-90) | 58 | 45 | .06 |

| Variable | Time to Patient Presentation | Time to Diagnosis | Time to Treatment |
|----------|-------------------------------|-------------------|-------------------|
|          | Median (days) | P            | Median (days) | P            | Median (days) | P            |
| Self-medication | .02 | .01 | .02 |
| No | 60 | 105 | 41 |
| Yes | 150 | 225 | 52 |
| Residence | .08 | .07 | .49 |
| Urban | 120 | 171 | 50 |
| Rural | 150 | 240 | 52 |
| Education | .77 | .71 | .07 |
| Illiterate | 150 | 220 | 55 |
| Literate | 135 | 214 | 45 |
| Awareness of risk factors | .73 | .31 | .37 |
| Unaware of risk factors | 150 | 220 | 55 |
| Aware of risk factors | 150 | 214 | 50 |
may be enhanced by collaboration with the traditional healers and community health volunteers to reduce various barriers and improve knowledge and trust. Current community health volunteers may be able to take on more of a patient navigator role, which is a patient-centered approach to improve health care delivery by promoting timely movement of a patient through a complex health care continuum adapted in many Western countries. Currently, this component of oncology care does not exist in Nepal. We do acknowledge that a limitation of this study was the dependence on patient and family recall for data on time intervals, and thus, recall bias must be kept in mind when interpreting the results. However, we feel the data are robust and the time intervals reflect what is seen in the clinic on a daily basis. These data allow us to move forward with future initiatives that will involve patient, family, and health care worker education at the community level.

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