original reports abstract

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

Soniya Dulal, MD, DM[1]; Bishnu Dutta Paudel, MD[1]; Lori Anne Wood, MD, MSc(Epi)[2]; Prakash Neupane, MD[3]; Aarati Shah, MD[1]; Bibek Acharya, MD[1]; Ramila Shilpakar, MD[1]; Sandhya Chapagain Acharya, MD[1]; Ambuj Karn, MD[1]; Bishal Poudel, MD[1]; Rameej Revanta Thapa, MBBS[4]; Albira Acharya, BE[5]; and Michael Gary Martin, MD[6]

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.

JCO Global Oncol 6:1258-1263. © 2020 by American Society of Clinical Oncology

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

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on July 9, 2020 and published at ascopubs.org/journal/go on August 7, 2020: DOI https://doi.org/10.1200/GO.20.00202

CONTEXT

Key Objective

Are there any factors that may contribute to delay in presentation, diagnosis, and treatment of GI cancers in Nepal?

Knowledge Generated

The time intervals for presentation, diagnosis, and treatment of cancer are longer in Nepalese patients with GI cancer compared with the intervals reported in other published literature from Western countries. The only baseline factor associated with greater delays was the use of self-medication.

Relevance

The results of this study could help guide infrastructure changes and educational initiatives to improve the time intervals and hopefully outcomes in Nepalese patients with GI cancers. Current community health volunteers may be able to take on more of a patient navigator role to improve health care delivery by promoting timely movement of a patient through a complex health care continuum.

context in Nepal.[4] 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.[5]

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 clinicopathologic 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.[6]

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

TABLE 1. Baseline Demographic and Clinical Characteristics of the Study Population

Characteristic	No. of Patients (%)[a]
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	65 (62.5)
IV	22 (21.2)
Prior awareness of risk factors of GI cancer	22 (21.2)
Use of self-medication	92 (88.5)

[a]Values are numbers and percentages, unless otherwise noted.

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.

TABLE 2. Presenting Symptoms

Symptoms	No. of Patients (%)		P
	Upper GI Cancer	Lower GI Cancer	
Abdominal pain	40 (83.3)	18 (32.1)	< .00001
Weight loss	33 (68.7)	34 (60.7)	.42
Vomiting	28 (58.3)	17 (0.3)	.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

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 *v* 143 days, respectively; $P = .62$), time to diagnosis (217 *v* 220 days, respectively; $P = .59$), or time to treatment (58 *v* 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 3. Types of Self-Medication

Medication	No. of Patients (%)			P
	Upper GI Cancer	Lower GI Cancer	Total	
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

TABLE 4. Time Intervals

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

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

TABLE 5. Association of Baseline Variables With Median Time Intervals in Days

	Time to Patient Presentation		Time to Diagnosis		Time to Treatment	
Variable	**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.[16] 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.

AFFILIATIONS

[1]Department of Clinical Oncology, National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal
[2]Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, Canada
[3]The University of Kansas Medical Center, Westwood, Kansas
[4]Damak Hospital, Damak-1, Jhapa, Nepal
[5]Kathmandu University, Kathmandu, Nepal
[6]West Cancer Center, University of Tennessee, Memphis, TN

CORRESPONDING AUTHOR

Soniya Dulal, MD, DM, Department of Clinical Oncology, National Academy of Medical Sciences, Bir Hospital, Kanti Path, Kathmandu 44600, Nepal; Twitter: @Soniya Dulal; e-mail: dulalsoniya1@gmail.com.

PRIOR PRESENTATION

Presented, in part, at the 55th Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 31-June 4, 2019; and the 56th Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 29-June 2, 2020.

AUTHOR CONTRIBUTIONS

Conception and design: Soniya Dulal, Bishnu Dutta Paudel, Prakash Neupane, Aarati Shah, Bibek Acharya, Ramila Shilpakar, Sandhya Chapagain Acharya, Michael Gary Martin
Collection and assembly of data: Soniya Dulal, Aarati Shah, Ramila Shilpakar, Ambuj Karn, Bishal Poudel, Rameej Revanta Thapa, Albira Acharya
Data analysis and interpretation: Soniya Dulal, Lori Anne Wood, Aarati Shah, Ramila Shilpakar, Albira Acharya, Michael Gary Martin
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/go/site/misc/authors.html.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Lori Anne Wood
Research Funding: Bristol Myers Squibb (Inst), Pfizer (Inst), Roche Canada (Inst), Exelixis (Inst), Merck (Inst), AstraZeneca (Inst), Novartis (Inst), Aragon Pharmaceuticals (Inst)

Prakash Neupane
Consulting or Advisory Role: Pfizer/EMD Serono
Research Funding: Merck Sharp & Dohme, Bristol Myers Squibb

Michael Gary Martin
Consulting or Advisory Role: AbbVie/Genentech, Jazz Pharmaceuticals

No other potential conflicts of interest were reported.

ACKNOWLEDGMENT

We acknowledge Ian F. Tannock, MD, PhD, DSc, Emeritus Professor of Medical Oncology, Princess Margaret Cancer Centre, Toronto, Ontario, Canada.

REFERENCES

1. Globocan, International Agency for Research on Cancer: Nepal. Summary statistic 2018. http://gco.iarc.fr/today/data/factsheets/populations/524-nepal-fact-sheets.pdf
2. Saito H, Takaya S, Fukumoto Y, et al: Clinicopathologic characteristics and prognosis of gastric cancer in young patients. Yonago Acta Med 55:57-61, 2012
3. Allgar VL, Neal RD: Delays in the diagnosis of six cancers: Analysis of data from the National Survey of NHS patients: Cancer. Br J Cancer 92:1959-1970, 2005
4. Marahatta SB, Shrestha A, Bhattarai PR, et al: TB: Barrier in access, diagnosis and treatment completion. J Manmohan Memorial Inst Health Sci 2:76-80, 2016
5. Piya MK, Acharya SC: Oncology in Nepal. South Asian J Cancer 1:5-8, 2012
6. Korsgaard M, Pedersen L, Laurberg S: Delay of diagnosis and treatment of colorectal cancer: A population-based Danish study. Cancer Detect Prev 32:45-51, 2008
7. Hosseini SN, Mousavinasab SN, Moghimi MH, et al: Delay in diagnosis and treatment of gastric cancer: From the beginning of symptoms to surgery—An Iranian study. Turk J Gastroenterol 18:77-81, 2007
8. Pita-Fernández S, González-Sáez L, López-Calviño B, et al: Effect of diagnostic delay on survival in patients with colorectal cancer: A retrospective cohort study. BMC Cancer 16:664, 2016
9. Tiwari V, Yogi V, Ghori HU, et al: Identifying the factors causing delayed presentation of cancer patients to a government medical college of Central India. J Clin Diagn Res 9:XC09-XC12, 2015

10. Adhikari B, Mishra SR, Babu Marahatta S, et al: Earthquakes, fuel crisis, power outages, and health care in Nepal: Implications for the future. Disaster Med Public Health Prep 11:625-632, 2017
11. Bergin RJ, Emery J, Bollard RC, et al: Rural–urban disparities in time to diagnosis and treatment for colorectal and breast cancer. Cancer Epidemiol Biomarkers Prev 27:1036-1046, 2018
12. Gillis A, Dixon M, Smith A, et al: A patient-centred approach toward surgical wait times for colon cancer: A population-based analysis. Can J Surg 57:94-100, 2014
13. Soni Kushwaha AK: Self-medication among cancer patients in Mahavir Cancer Sansthan, Patna. J Clin Exp Pharmacol 9:260, 2019
14. Kadayat TM, Parajuli A, Bist G, et al: Complementary and alternative medicine in Nepal: A case study. J Med Use Dev Countries 1:3-13, 200
15. Tata MD, Dharmendran R, Ramesh G, et al: Delay in diagnosis of upper gastrointestinal cancer: Whose fault is it? Med J Malaysia 68:275-277, 2013
16. Meade CD, Wells KJ, Arevalo M, et al: Lay navigator model for impacting cancer health disparities. J Cancer Educ 29:449-457, 2014