

Time Intervals From Onset of Clinical Manifestations to Treatment in Patients With Cancer at Hospital General San Felipe, Tegucigalpa, Honduras

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PURPOSE In cancer, clinical staging is related to outcomes, and this is linked to the evolution of the disease over time. In Honduras, cancer mortality is high, and time intervals from onset of symptoms to treatment of cancer are not known. We conducted a cross-sectional study to determine these intervals.

PATIENTS AND METHODS This investigation was carried out from April 25 to August 30, 2018, and included 202 patients at the main cancer referral center in Honduras. For the purposes of the study, information was obtained from patients, their caregiver, medical records, or treatment cards. Patients older than age 18 years were included after informed consent was signed.

RESULTS The mean time interval from onset of symptoms to cancer treatment was 232 days. Different intervals of time were identified, and the mean of these intervals was calculated in days as follows: 68 days from onset of symptoms to first medical evaluation; 146 days from first evaluation to oncologist consultation; 26 days from cancer specialist to the pathology report; and 86 days from the histopathologic diagnosis to the beginning of treatment. Once diagnosis was established, the average elapsed times to chemotherapy, radiotherapy, surgery, and chemoradiotherapy were 88, 102, 76, and 154 days, respectively ($P < .05$, when surgery is compared against chemotherapy and radiotherapy).

CONCLUSION The mean time interval from symptom presentation to treatment in patients with cancer is more than 7 months. This could explain the advanced stages of disease seen at the time of treatment in Honduras, which decrease chance of cure and increase the mortality rate of cancer. Appropriate intervention to decrease these intervals must be taken to reduce mortality.

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INTRODUCTION

Cancer is the second leading cause of death worldwide, after cardiovascular disease. The global incidence of cancer increased 33% between 2005 and 2015, and 70% of deaths occur in low- or middle-income countries.^{1,2} According to GLOBOCAN, by the year 2030, 24.1 million patients with cancer and 13.0 million deaths are expected globally. In Latin America, by 2030, 1.7 million patients with cancer and 1 million deaths are expected if prevention, early diagnosis, and timely treatment interventions are not enacted.³

The high mortality attributed to cancer in low- and low-to middle-income countries involves several factors, including inadequate and obsolete infrastructure, limited human resources, and limited therapeutic modalities related to the health system.^{4,5} Furthermore, patient-related factors that contribute to the higher cancer mortality rate include the nature and importance assigned to the symptoms that might

indicate the presence of a cancer; fear, myths, and beliefs about the disease; and physical, social, and psychological barriers. All of these factors lead to more advanced clinical stages of diseases at presentation.⁶⁻⁸

Honduras is a low- to middle-income country in which the cancer incidence is increasing annually, constituting a serious health problem.^{9,10} The Global Cancer Observatory estimated 9,942 new cancers and 5,964 deaths (59.99%) by the year 2018, with a projection for the year 2030 of 14,937 cancers and 9,054 deaths (60.61%).³

Honduras encompasses 112,492 km² and has 9,105,903 inhabitants. The Honduran public health system consists of 30 state hospitals distributed in 18 departments that serve more than 60% of the population.^{11,12} Cancer management is provided in two of these 30 hospitals, one in San Pedro Sula and a second in Tegucigalpa (Hospital General San Felipe). To further document the incidence and prevalence of

ASSOCIATED CONTENT

Appendix

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

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CONTEXT

Key Objective

Is it possible to know the time interval from the onset of clinical manifestations to oncologic treatment in patients with cancer in Honduras?

Knowledge Generated

In Honduras, the time elapsed from the onset of clinical manifestation to specific treatment in patients with cancer is more than 7 months, a longer period than is seen in high-income countries.

Relevance

This long time interval could explain why patients with cancer in Honduras are in advanced stages of disease at the time when treatment is established, affecting outcomes and decreasing survival. On the basis of the findings of this study, health strategies and interventions should be instituted to reduce this time interval in order to improve treatment outcomes and reduce cancer mortality.

the factors that lead to worse cancer outcomes in Honduras, we conducted a study to determine the interval from onset of first symptoms to treatment in patients diagnosed with cancer in Hospital General San Felipe.

PATIENTS AND METHODS

A descriptive cross-sectional study was performed, including 202 patients diagnosed with cancer who were hospitalized in the medical oncology and surgical oncology wards of Hospital General San Felipe in Tegucigalpa, Honduras, during the period between April 25 and August 30, 2018. Information was obtained by questioning the patients and reviewing the clinical records and treatment control cards. The data were collected using a 24-question instrument designed for that purpose (Appendix Table A1).

Demographic characteristics, economic information, and information on onset of symptoms, first medical evaluation, and the oncologist's consultation were obtained from the patient or caregiver. Information about date and type of clinical diagnosis, clinical stage, extension studies, surgical treatment, verification of the histopathologic diagnosis, and date of pathology report was obtained from the medical record. Chemotherapy, radiotherapy, and chemoradiotherapy treatments were verified using the respective treatment card of each patient.

Eligibility criteria included age greater than 18 years, ability to respond to the questions, and ability to provide informed consent. If the patient was unable to provide the requested information, it was obtained from the patient's caregiver. Patients younger than age 18 years or those who declined to participate were excluded.

This research was approved by the Department of Teaching and Research of the Hospital General San Felipe. The analysis of data was performed using Epi Info version 7.2 (Centers for Disease Control and Prevention, Atlanta, GA) and Microsoft Office Excel 2016 (Microsoft, Redmond, WA) programs and the R 1.1.456 program for statistical analysis.

RESULTS

Demographics

Two hundred two patients diagnosed with cancer at Hospital General San Felipe were enrolled in this study, including 139 women and 63 men, with a mean age of 52 years (Table 1). The types of cancer were categorized by anatomic distribution as follows: female urogenital; digestive and hepatobiliary; head and neck; colorectal; skin, muscle, and bone; male urogenital; respiratory tract; hematologic; and unknown primary tumor.

Of the 202 patients, 193 patients (95.54%) sought medical attention initially as a result of symptoms or signs of their diseases, and nine patients (4.46%) sought medical attention because of findings on x-ray imaging studies or cervical cytology. The vast majority of health providers responsible for the first evaluation were general doctors (n = 111, 54.95%). Other specialists who first saw the patients included gynecologists (n = 22, 10.89%), internists (n = 22, 10.89%), general surgeons (n = 15, 7.43%), gastroenterologists (n = 4, 1.98%), medical oncologists (n = 3, 1.49%), dermatologists (n = 3, 1.49%), orthopedists (n = 3, 1.49%), radiologists (n = 2, 0.99%), and a surgical oncologist, a radiation oncologist, a cardiologist, and an otolaryngologist (n = 1 each, 0.5%). Twelve patients (5.94%) were evaluated by nonmedical personnel, such as nurses and naturalists.

The most frequent symptoms that led patients to seek medical attention and the associated cancer category are listed in Table 2. The most common presenting symptom was pain (n = 89, 44.06%). Less common reasons for seeking care included self-detected palpable tumor (n = 62, 30.69%), bleeding (n = 25, 12.38%), unexplained weight loss (n = 14, 6.93%), and GI abnormalities (n = 12, 5.94%). As can be seen in Table 2, the specific symptoms were related to specific diseases. For example, digestive, hepatobiliary, female urogenital, and colorectal cancers presented with many of these findings, whereas malignancies of the head and neck and sarcomas were almost

TABLE 1. Demographic Data of Patients Diagnosed With Cancer at Hospital General San Felipe, Tegucigalpa, Honduras

Factor	No. of Patients (N = 202)	%
Mean age, years (range)	52 (19-87)	
Sex		
Female	139	68.81
Male	63	31.19
Education		
Literate	171	84.65
Illiterate	31	15.35
Occupation		
Housewife	98	48.51
Unemployed	22	10.89
Farmer	21	10.40
Merchant	16	7.92
Other occupation	45	22.28
Monthly income, \$		
< 367.46*	177	87.62
> 367.46	25	12.38
Cancer category		
Female urogenital	70	34.65
Digestive and hepatobiliary	36	17.82
Head and neck	28	13.86
Colorectal	23	11.39
Skin, muscle, or bone	18	8.91
Male urogenital	12	5.94
Respiratory tract	10	4.95
Hematologic	3	1.49
Unknown primary tumor	2	0.99
Ward		
Surgical oncology: women	84	41.58
Surgical oncology: men	26	12.87
Medical oncology: women	55	27.23
Medical oncology: men	37	18.32

*Income is shown in US dollars; this value corresponds to the Honduras minimum wage (8,448 lempiras monthly).

exclusively brought to the patient's attention by the presence of a palpable mass.

The doctors responsible for oncologic evaluations of the 202 patients included the following specialties: surgical oncology (n = 111 patients, 54.95%), medical oncology (n = 85 patients, 42.08%), and hematology, mastology, pneumology, gynecologic oncology, and radiation oncology (n = 1 patient each). For one patient, the service was unknown.

Time to First Treatment

The mean elapsed time from first clinical manifestation to oncologic treatment of the 202 eligible patients was

232 days (Table 3). The mean time between symptom onset and seeing any health provider was 68 days (range, 1 to 730 days). Moreover, the mean time from first symptom to evaluation by a cancer specialist was 147 days (range, 1 to 766 days).

Only 178 of 202 patients (88.12%) had a biopsy report in their medical record. Of these 178 patients, the biopsy was performed in 85 (48%) before the patient was evaluated by a cancer specialist. Of 79 patients who did not have a biopsy before seeing a cancer specialist and for whom it was possible to determine, the mean time elapsed from cancer specialist evaluation to obtaining the biopsy report was 26 days (range, 1 to 120 days). For 14 patients, the date of the biopsy report was illegible, and for 24 patients, information could not be found.

The mean time elapsed after obtaining a biopsy report to initiation of specific treatment was 86 days (range, 1 to 858 days). Mean time to treatment initiation was longer for patients who had the biopsy before versus after being evaluated by an oncologic specialist (54 days [range, 1 to 187 days] v 27 days [range, 1 to 106 days], respectively; $P < .001$).

Some form of cancer treatment was initiated in 123 patients, and 79 patients had not received treatment when the study was closed. The reason why patients had not received treatment was beyond the objective of this study.

For patients whose date of beginning of treatment was possible to determine, the mean time elapsed for specific modality was as follows: surgery (n = 49), 7 days (range, 1 to 858 days); chemotherapy (n = 41), 88 days (range, 1 to 173 days); radiotherapy (n = 10), 102 days (range, 1 to 297 days); and simultaneous chemoradiotherapy (n = 5), 154 days (range, 1 to 603 days).

When comparing the elapsed time to perform surgery versus the time to start chemotherapy or radiotherapy, the time interval between diagnosis and treatment was significantly shorter for surgery ($P < .05$), whereas the difference in time was not significant between chemotherapy and radiotherapy ($P = .9$; Kruskal-Wallis test). When comparing the time interval from onset of symptoms to treatment in patients who had an ordered sequence of evaluation (meaning from general practitioner, oncologist's consultation, or biopsy report to treatment) versus those who did not have an ordered sequence, the difference was not statistically significant ($P = .84$; Fig 1)

DISCUSSION

In Honduras, cancer mortality is higher than in high-income countries, such as the United States or the United Kingdom. The causes of this disparity have not been determined, but one is likely to be delayed diagnosis, with an accompanying advanced state of disease before oncologic treatment is initiated.^{4,13} We observed that the time interval from first clinical manifestations to specific treatment in

TABLE 2. The Most Frequent Symptoms in Patients and Their Relationship to Cancer Category and Interval of Time to First Clinical Evaluation

Symptom and Cancer Category	Total No. of Patients (N = 202; %)	% of Patients With Symptoms	Mean No. of Days From Onset of Symptom to First Clinical Evaluation (range)
Pain	89 (44.06)		54 (0-696)
Digestive/hepatobiliary		24.72	
Female urogenital		24.72	
Colorectal		15.73	
Palpable tumor	62 (30.69)		92 (0-730)
Female urogenital		45.90	
Head and neck		21.30	
Skin, muscle, and bone		18.03	
Bleeding	25 (12.38)		52 (0-275)
Female urogenital		50.00	
Digestive/hepatobiliary		20.83	
Colorectal		20.83	
Weight loss	14 (6.93)		123 (15-696)
Digestive/hepatobiliary		28.57	
Colorectal		28.57	
Respiratory tract		21.43	
Diarrhea or constipation	12 (5.94)		47 (15-120)
Colorectal		66.67	
Digestive/hepatobiliary		16.67	
Female urogenital		8.33	

Honduras is greater than 7 months. These data are similar to those in other low-income countries and stand in contrast to those reported in high-income countries, in which the interval is 1 to 2 months.^{8,14,15}

We also observed that the average interval from the onset of clinical manifestations to the first medical evaluation was approximately 9 weeks (68 days), again distinctly in contrast to the interval of 2 weeks found in other countries.¹⁶ Moreover, the first medical evaluation was carried out mostly by general practitioners (55%) or by doctors of

diverse medical specialties (45%), indicating that there is not a rigid system of public health attention in Honduras. Surprisingly, following an ordered sequence did not decreased the time to cancer treatment initiation (Fig 1), probably because of multiple medical evaluations before oncologist consultation, time of referral to cancer specialist, and delays in obtaining diagnostic test results or in initiation of treatment.

We also found that pain, tumors, bleeding, weight loss, and changes in bowel habits were the most common symptoms

TABLE 3. Time Intervals Between Clinical Manifestations of Cancer and Treatment

Interval	No. of Patients (%)				Total No. of Patients	Mean Time (days)
	≤ 30 Days	31-90 Days	≥ 91 Days	UD		
IST1	87 (43.07)	32 (15.84)	48 (23.76)	35 (17.33)	202	67.84
IST2	58 (28.71)	42 (20.79)	86 (42.57)	13 (6.44)	199	146.57
IST3	64 (31.68)	8 (3.96)	7 (3.47)	14 (6.93)	93	25.63
IST4	46 (22.77)	30 (14.85)	22 (10.89)	9 (4.46)	107	85.52

NOTE. Table does not included the following information: three patients (1.49%) went directly to the cancer specialist; 24 patients (11.88%) had not been biopsied when they were referred, whereas 85 patients (42.08%) had been biopsied; 79 patients (39.11%) had not begun treatment with an average time elapsed of 101.63 days; and 16 patients (7.92%) had begun treatment before receiving a histopathologic diagnosis.

Abbreviations: IST1, mean time between symptom onset and seeing any health provider; IST2, mean time from first symptom to evaluation by a cancer specialist; IST3, mean time elapsed from cancer specialist evaluation to obtaining the biopsy report; IST4, mean time elapsed after obtaining a biopsy report to initiation of specific treatment; UD, undefined (patients did not remember dates).

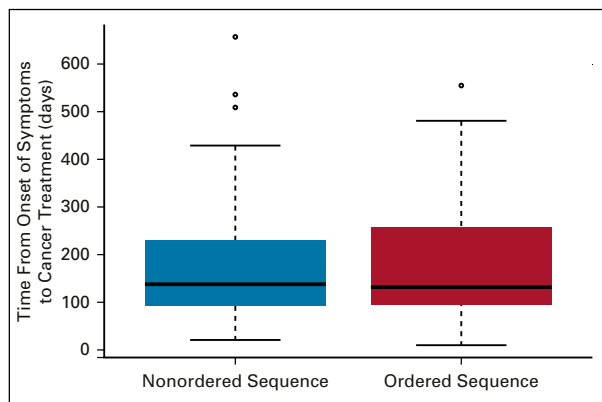


FIG 1. Time interval from onset of symptoms to cancer treatment comparing a nonordered sequence with an ordered sequence of evaluation. An ordered sequence means that patients followed an expected order from general practitioner to oncologist consultation to biopsy report, and finally to treatment.

frequently associated with cancer. Indeed, major cancer health outcomes were dramatically improved in high-income countries such as the United States when celebrities, such as First Lady Betty Ford (breast cancer) and President Ronald Reagan (colon cancer), openly discussed the importance of recognizing the signs of cancer and bringing them to the attention of a health provider immediately. Our data suggest that public health education in Honduras should be focused on such a campaign.^{8,16}

However, even when patients sought medical care, our results demonstrated a delay of approximately 21 weeks (147 days) before evaluation by a cancer specialist. The reasons for this delay were not determined but could represent an inadequate referral system, lack of knowledge of the general practitioner, or an insufficient number of facilities and cancer specialists.^{4,8,16,17}

We also identified a major inconsistency with regard to when biopsies were obtained and reported. Importantly,

patients with a biopsy report obtained before being evaluated by a cancer specialist started treatment much more quickly than those whose biopsy report was not available ($P < .001$). More than one half of patients were seen before they had a biopsy or before the report was available, and in 14 patients, the report dates were not legible. Regardless, the mean time interval to start any oncology treatment was 86 days, more than 12 weeks after the biopsy report was obtained; this is a substantial delay in initiating therapy and, presumably, caused worse outcomes.^{18,19}

However, pathology reporting was not the only factor involved in treatment delay. For example, although patients experienced less of a delay to undergo surgery compared with starting chemotherapy or radiotherapy, the time interval from pathologic report to surgery was still 10 weeks. Likewise, even after pathologic diagnosis was established, the time interval to start chemotherapy was approximately 3 months. Taken together, these long delays to treatment, which were as long as 6 months from the time of biopsy and pathologic diagnosis, may negatively affect the probability of survival.^{19,20,21}

This study shows that the time interval from onset of symptoms to treatment in patients with cancer at the main referral center for cancer treatment in Honduras is prolonged compared with what is the standard of care in high-income countries. This delay is likely to be responsible for the high cancer mortality in this country. We maintain that such delays are unacceptable, given the greater cancer morbidity and mortality as a result of the decrease in effectiveness when therapies are initiated later compared with earlier in the disease process. The greater morbidity and mortality affect not only patient quality and length of life, but also increase downstream cultural and economic adversity. Our data strongly suggest that appropriate measures must be taken to reduce the time to initiate cancer therapy in Honduras.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Travel, Accommodations, Expenses: Asofarma

No other potential conflicts of interest were reported.

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APPENDIX

TABLE A1. Variables Included in the Questionnaire Instrument

Variable
File No.*
Age†
Sex
Residence†
Education†
Marital status†
Occupation†
Socioeconomic status (monthly income)†
No. of live children†
Date of first clinical manifestation†
Type of first clinical manifestation†
Date of first clinical evaluation†
Type of first clinical evaluation†
Date of first specialized evaluation†
Type of first specialized evaluation†
Date of histopathologic diagnosis*
Type of histopathologic diagnosis*
Clinical diagnosis*
Clinical staging*
Start of treatment*†‡
Date of first treatment*†‡
Type of treatment*†‡
Purpose of treatment*
Additional examinations and annotations*

*Extracted from the clinical record.

†Provided by the patient.

‡Extracted from the treatment card.