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The prevalence and correlates of comorbidities among patients with cancer attending a tertiary care cancer center in South India: An analytical cross-sectional study

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Abstract

Background—Comorbidities in patients with cancer can affect treatment, and should, therefore, be prioritized and managed.

Objectives—Our primary aim was to assess the prevalence of comorbidities among patients with cancer. The secondary objective was to identify the association of comorbidities with various sociodemographic and clinical variables.

Materials and Methods—This was a cross-sectional study conducted between December 2019 and March 2020 among patients with cancer, seeking treatment at Malabar Cancer Center, in Kannur District of northern Kerala in South India. Semi-structured interviews were conducted, and comorbidities were assessed using the Charlson Comorbidity Index. The anthropometric measurements were recorded using a standardized instrument and protocol.

Results—We enrolled 242 patients in this study. There were 148 (61.2%) female patients; 106 (43.8%) were aged between 41 and 50 years. Cancers of the head-and-neck and breast accounted for the majority of cases (23.1% each, $n = 56$), followed by the digestive system (18.6%, $n = 45$) and female reproductive system (11.2%, $n = 27$). The most common primary cancers in the head-and-neck, digestive, and female reproductive systems were oral, colorectal, and cervical, respectively. The prevalence of comorbidities among patients with cancer was 70.2% ($n = 170$).

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Author contributions
Conception or design of the work: DS, EM; data collection: DS; data analysis and interpretation: DS, JJ; drafting the article: JJ; critical revision of the article: EM; final approval of the version to be published and accountability for all aspects of the work: all authors.

Conflicts of interest
There are no conflicts of interest.

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Common comorbidities were hypertension (*n* = 82 ; 33.9%), arthritis (*n* = 57; 23.6%), and diabetes (*n* = 53; 21.6%). After controlling for potential confounders, the factors noted to be independently associated with the presence of comorbidities were advanced age, family history of comorbidity, normal weight or underweight, and cancer treatment for more than 6 months' duration.

Conclusions—The high prevalence of comorbidities among patients with cancer suggests the need for an integrated system of care and management as the comorbidities affect the overall management of cancer treatment and care.

Keywords

Cancer; comorbidity; malignancy; neoplasms; tumor

Introduction

Non-communicable diseases are the leading cause of death worldwide.[1] Of all the non-communicable diseases, cancer is the second leading cause of death worldwide.[1] Cancer deaths are expected to rise to 11 million by the year 2030.[2] It is estimated that nearly half the new cancer cases and more than half the cancer deaths worldwide occurred in Asia in 2018.[3] The available data suggest that there is an alarming increase in the burden of cancer in India in recent years.[4] An early diagnosis is important to improve the outcome of patients with cancer.[5] Various factors contribute to delays in the diagnosis of cancer, including the type and severity of comorbidities, lack of awareness,[6] perceived stigma related to the illness,[7,8] and poor access to health services.[9,10]

Comorbidities are critically important in the care of patients with cancer because they can have a profound impact on many aspects of care, from prevention, screening, and diagnosis to prognosis, treatment, and health service needs.[11]

The interaction of comorbidities such as diabetes, hypertension, hyperlipidemia, and other non-communicable diseases is one of the major challenges in cancer treatment and survivorship.[6] Comorbidities have both positive and negative impacts on cancer treatment outcomes. For example, the presence of comorbidities provides an opportunity for screening and early diagnosis leading to greater access to health services.[11] At the same time, comorbidities could prevent the establishment of a thorough and complete diagnosis due to challenges in performing high-level or highly invasive diagnostic tests,[11] leading to diagnostic delays.[12] Furthermore, recent evidence suggests the role of comorbidities in cancer development and tumor biology.[13] All these factors could adversely affect the diagnosis, treatment options, prognosis, and outcomes.[13] Cancer survivors with comorbidities must manage both cancer and their comorbidities which tend to increase as they live longer.[14] Moreover, comorbidities and their management impose an additional economic burden which increases the healthcare expenditure.[15]

It is, therefore, imperative to understand and manage the comorbidities of patients with cancer. In contradistinction to the large number of studies done on the core issues of cancer, there have been very limited research studies done globally, as well as in India, on

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comorbidities in patients with cancer.[16,17] Hence, there is a need for data from India to assess the prevalence and distribution of comorbidities among patients with cancer.

Materials and Methods

General study details

This was an analytical cross-sectional study conducted in the outpatient clinic among patients with cancer, seeking treatment at Malabar Cancer Center (MCC), a tertiary cancer care facility in Kannur District, southern India from December 2019 to March 2020. The study was approved by the Institutional Human Ethics Committee (CUK/IHEC/2019/037) on December 02, 2019 [Supplementary Appendix 1]. Written informed consent was obtained from all participants prior to enrolment in the study. This study was not registered in a publicly accessible clinical trials registry like the Clinical Trials Registry of India as it was not a clinical trial. The study was conducted in accordance with the ethical guidelines established by the Declaration of Helsinki, and those established by the Indian Council of Medical Research. The privacy and confidentiality of the participants were maintained. There was no funding for this study.

Participants

We included patients aged 18–70 years, with a clinical or histologic diagnosis of cancer, who were undergoing treatment and had visited the outpatient department of MCC. We excluded critically ill subjects and those who refused to provide informed consent.

Objectives

The primary objective was to evaluate the prevalence of comorbidities among patients with cancer undergoing treatment. The secondary objective was to identify the association of comorbidities with selected sociodemographic and clinical variables of patients with cancer undergoing treatment.

Study methodology

All eligible subjects during the data collection period were recruited consecutively from the outpatient clinics of the oncology departments. A systematic random sampling was employed for participant selection, with every third person in the outpatient department identified as a study participant.

A structured questionnaire was used [Supplementary Appendix 2], which included sociodemographic information, medical history, family history, type of cancer, and duration of treatment. Comorbidities were assessed using the Charlson Comorbidity Index,[18] which categorized comorbidities based on the International Classification of Diseases (ICD). The presence or absence of any one of the 19 listed comorbid conditions was identified through the interview and available patient medical records.[19] Though the Charlson Comorbidity Index score can be used to estimate the 10-year expected survival rate in patients with multiple comorbidities, we used it only to identify comorbidities. The tool was first translated to the local language (Malayalam) and then back-translated. Pretesting

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of the tool was done to assess feasibility, comprehensibility, time taken to complete, and standardization of the questions.

The structured questionnaire was administered during an interview by the first author (DS) in the local language, after obtaining informed consent from the participants and ensuring adequate privacy in the outpatient department setting. The interviews lasted 20 to 30 minutes per patient.

Anthropometric measurements such as height (in meters) and weight (in kilograms) were recorded using standardized instruments. The standard protocol was used for measuring height and weight as per the World Health Organization.[20] Body mass index (BMI) was calculated using the formula: weight in kilograms divided by the square of height in meters. Physical activity was assessed using a question "Were you physically active prior to the diagnosis of cancer?" The patients' socioeconomic status was assessed as per the revised Kuppuswamy scale.[21] The education was captured as professional, graduate, postgraduate, high school, middle school, primary education, and illiterate. Each of these was given scores from 1 to 7. Under the professional category within education, we included, any higher professional education like medicine (MBBS), masters' degrees (master's in arts, sciences, humanities, and education), engineering degrees (bachelor's degree in engineering or architecture), etc., We included bachelor's degrees in arts, science, and humanities in the undergraduate section. Class 12 with vocational diploma was also included as post-high school. High school education included Class 10 pass/Class 11 pass. Individuals who had passed Classes 8 or 9 were considered to have received a middle school education. Any individuals who had education up to 7^{th} grade were included as primary educated. People who could only read but not write with understanding were included in the illiterate category. The occupation was captured as professional, semi-professional, clerical/shop owner/farmer, skilled worker, semi-skilled worker, unskilled worker, retired, and unemployed. Jobs included under professionals were doctors, engineers, architects, directors, senior administrators, bank employees, bank officers, and college teachers. Semi-professional jobs included school teachers, junior administrators, and junior medical practitioners. The third occupation category (clerical/shop owners/farmers) included clerks/accountants, farm owners, salesmen, insurance agents, and news journalists. Skilled workers included telephone operators, masons, carpenters, and mechanics. Semi-skilled workers were factory laborers, car cleaners, and petty shopkeepers. Unskilled workers were domestic servants, peons, watchmen, and other unskilled daily wage earners.

Definitions

Comorbidity referred to a long-term health condition in the presence of the primary disease of interest, i.e., cancer.[19] Multimorbidity was defined as the co-occurrence of two or more comorbidities.[22]

Statistics

We estimated the sample size using the formula, 3.84 pq/d2. In this formula, "p" denotes the prevalence of the condition/health state, where "p" is expressed in terms of percentage, "q" = 100-p and "d" is the precision or absolute error.[23] Salako *et al.*[24] reported that

the prevalence of comorbidities among patients with cancer was 26.9% in Uganda. As this was the only available prevalence rate at the time of the study, and there was no available literature from India, we used this prevalence rate for the sample size calculation.[24] The sample size of 242 was obtained with a p of 26.9%, q of 73.1 (100-26.9), an optimum precision of 6% and a non-responsive rate of 10% to account for unwillingness or incomplete data.

The data were entered into Microsoft Excel 2010 version and analyzed by using the Statistical Program for the Social Sciences (SPSS) software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Descriptive statistics were performed where appropriate, followed by bivariate analysis to explore the association between the variables. Binary logistic regression was done to understand the correlates of comorbidities. $P < 0.05$ was considered statistically significant.

Results

Participant enrolment

Out of the total 260 patients screened for the study, 242 consented to provide the required data and were included in the present study [Figure 1].

Sociodemographic and clinical profile of the participants

The majority of the participants were in the age group 41–50 years ($n = 106$, 43.8%) and 148 (61.2%) were women. The most common cancers were head-and-neck ($n = 56$; 23.1%) and breast cancer ($n = 56$; 23.1%). Nearly 40% ($n = 103$) of the study subjects had been on cancer treatment for less than a month. The characteristics of the study participants are shown in Table 1.

Prevalence of comorbidities and multimorbidities

Comorbidities were noted in 170 patients (70.2%; 95% confidence interval [CI], 64.1–75.9). There were 91 patients (37.6%; 95% CI, 31.5–44.0) who had multimorbidities. The most common comorbidity was hypertension ($n = 82$; 33.9%) followed by arthritis ($n = 57$; 23.6%), and diabetes ($n = 53$; 21.6%). Stroke ($n = 3$; 1.2%) and cognitive impairment ($n = 2$; 0.8%) were uncommon in our study population. Except for cardiovascular diseases (CVDs) and depression, all the other comorbidities were present prior to the diagnosis of cancer.

Correlates of comorbidities

The distribution of comorbid illnesses among patients with cancer is provided in Table 2. After controlling for potential confounders, the overall logistic regression model [Table 3] showed that advancing age (51–70 years; adjusted Odds ratio [OR], 5.96; 95% CI, (2.84-12.50), normal weight or underweight (adjusted OR, 2.85 95% CI, 1.26-6.43), and receiving cancer treatment for more than 6 months duration (adjusted OR, 4.06; 95% CI, 1.77-9.31) were independently associated with the presence of comorbidities among patients with cancer.

Discussion

We found that the prevalence of comorbidities among patients with cancer, seeking treatment at our tertiary care center in South India was 70.2% (*n* = 170). Hypertension was the most common comorbidity (*n* = 82, 33.9%) followed by arthritis (*n* = 57, 23.6%), and diabetes mellitus (*n* =67.9, 21.9%). Data on comorbidities among patients with cancer are sparse and vary greatly across the globe. A meta-analysis from China reported that 42.4% of patients with cancer had hypertension.[25] A study conducted in Nigeria reported the most common comorbidities in patients with cancer were hypertension (20.4%, *n* = 173), diabetes mellitus (6.7%, *n* = 53), and peptic ulcer disease (2.1%, *n* = 18).[24] Similar results to those generated in our study were reported from a study in the United States of America (USA), which showed that 68.7% (*n* = 10735) of patients with cancer had comorbidities.[26] Thus, we found that the prevalence of comorbidities among patients with cancer in Kerala was relatively similar to that in developed countries.

We found that 91 (37.6%) of the participants had been diagnosed with two or more comorbidities in addition to cancer, which was similar to the reported figure of 32.6% (*n* = 5094) prevalence of multimorbidity in the USA.[26] Other regions such as Denmark reported a multimorbidity prevalence of 27% (*n* = 70671) among patients with cancer.[27] This could be because our study was conducted in the Indian state of Kerala, which is considered the most advanced state in epidemiological transition.[28] Epidemiological transition refers to the changing pattern of population distribution with respect to changing patterns in mortality, fertility, life expectancy, and causes of death. The state of Kerala, unlike other Indian states, has the highest reported prevalence of most chronic diseases and their risk factors,[28] despite the reduced fertility rates and increased life expectancy. It is important to note, however, that the identification of comorbidities is essential, as they have been shown to result in a higher risk of mortality and reduced quality of life.[29]

The association between comorbidities and advancing age is plausible because most of the biological pathways leading to chronic diseases take a long time to affect individuals.[30] The prevalence of comorbidities was 47.4% (*n* = 81) among older adults (60–70 years) compared to younger age groups of 30–39 years (1.2%, *n* = 2), 40–49 years (14.6%, *n* = 25), and 50–59 years (36.8%, *n* = 63). Similar to our findings, another study reported a higher prevalence of comorbidities in older adults (70–79 years).[31,32] This association may be attributed to the fact that obese and overweight people are at greater health risk due to their lifestyle, nutrition, and physical activity.[33] Irrefutable evidence suggests that overweight and obesity were associated with various chronic illnesses including cancer. However, our study on patients with cancer showed that those with normal weight and below were more likely to have comorbidities. This could be a reflection of the weight loss and debility resulting from cancer. The cross sectional nature of the study limited our understanding of the bi-directional nature of occurrence of events.[34]

Our findings underline the need to shift the focus of research from disease-specific treatments and patients with single diseases to studies that include patients with comorbidities/multimorbidity. The high prevalence of multimorbidities among patients with cancer warrants immediate attention of healthcare professionals in treating the co-occurring

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conditions which, if not addressed, can affect the quality of life, and predispose to functional limitations.[35]

We found that age was a significant predictor of comorbidities and multimorbidity in patients with cancer. Hence, cancer care should include screening for comorbidities, predominantly among those persons who present with cancer beyond middle age as these conditions are more prevalent in older age groups. The coexistence of comorbidities in patients with cancer calls for a multifaceted approach to cancer care and management and implementation of effective strategies to improve the patients' quality of life.[36–38] Furthermore, considering the high proportion of undiagnosed chronic diseases in the Indian population, it is critical that patients diagnosed with cancer are screened for other common non-communicable diseases and that they receive holistic chronic disease care and management.

In the current study, we explored the prevalence and distribution of comorbidities among patients with cancer. This knowledge might assist in planning and improving healthcare services. A limitation of our study was that we captured only the self-reported comorbidities using the Charlson Comorbidity Index and did not perform any confirmatory tests. Furthermore, the study cohort was limited to treatment-seeking patients with cancer who were available during the study period. As the study was done in the only cancer care facility in North Kerala, the patients who sought care represent the vast majority of patients with cancer. However, the study results are limited to those who seek and had access to health care. The cross-sectional nature of the study imposed a limitation on the temporality of the events.

Conclusion

Almost three-quarters of patients with cancer have comorbidities. It is imperative that oncologists take cognizance of underlying comorbidities and provide holistic care to patients. The knowledge generated from this study will form the mainstay for proper healthcare planning for people living with cancer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Nil.

Data sharing statement

Individual deidentified participant data will be shared on request by Dr. Elezebeth Mathews, dr.elezebethmathews@cukerala.ac.in. Particular participant data will not be shared. The study protocol has already been made available. The data will be made available up to 6 months after publication. The data will be provided in case any author has any queries or needs this information for further study.

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Putting in Perspective

Central question

- What is the prevalence of comorbidities among patients with cancer?

Key findings

- Nearly two-thirds (n = 170, 70.2%) of patients with cancer had comorbidities.
- One-third (n = 91, 37.6%) of patients with cancer had multiple comorbidities.
- Advanced age, normal or below-normal body mass index (BMI), and treatment duration longer than six months significantly correlated with the presence of comorbidities.

Impact

- There is a huge burden of comorbidities among patients with cancer, which adds to the burden of care and management for cancer, and impacts the responsiveness to therapy.
- Identification of comorbidities among patients with cancer would enable better management of comorbidities, thereby increasing the uptake of cancer treatment and its tolerance.
- There is a need for healthcare professionals to recognize and treat co-occurring conditions along with cancer therapy, which, if not addressed, can affect the quality of life and predispose to functional limitations.

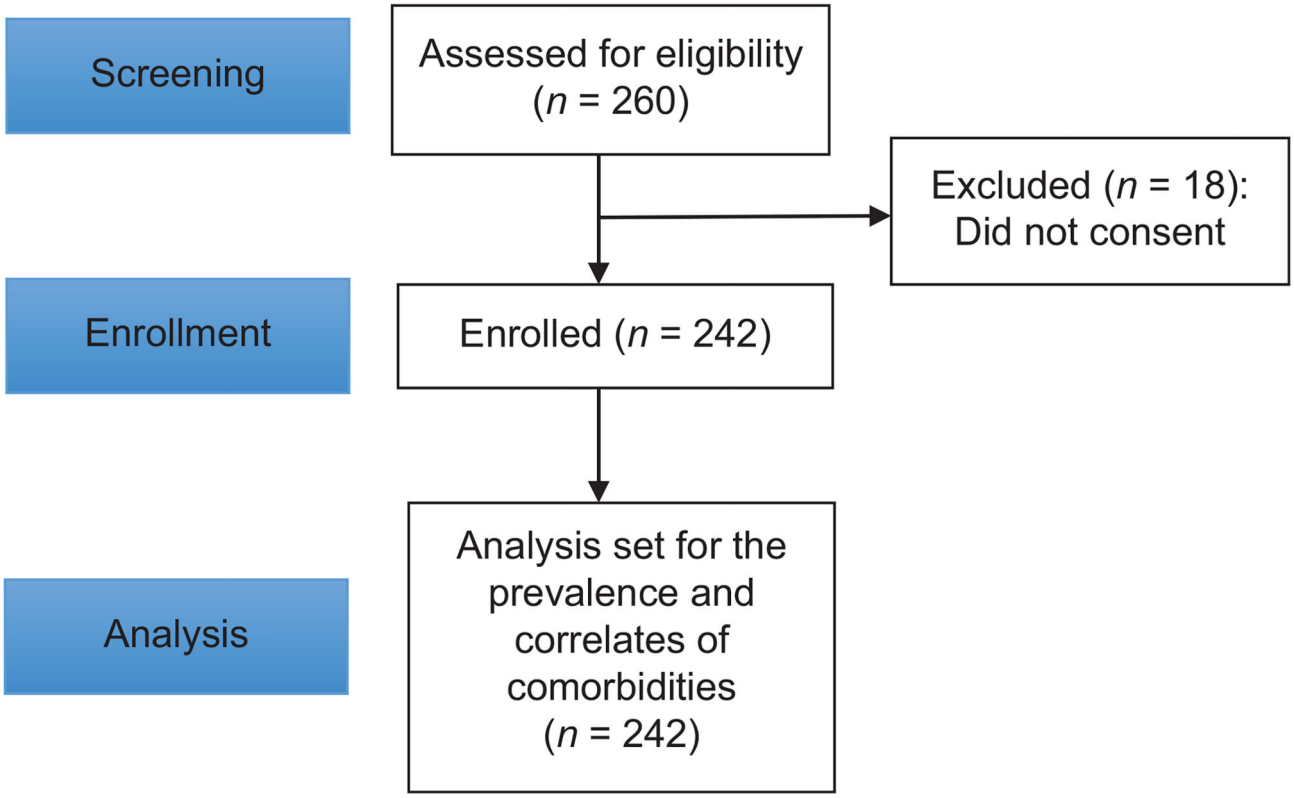

Figure 1. Flowchart of the selection criteria for patient recruitment

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Table 1
Sociodemographic and clinical profile of the subjects

Variables	Sub-categories	Number of patients (%) *n*=242
Age (in years)	<30	10 (4.1)
	31-40	48 (19.9)
	41-50	106 (43.9)
	51-60	68 (28.0)
	61-70	10 (4.1)
Sex	Male	94 (38.8)
	Female	148 (61.2)
Religion	Christian	52 (21.5)
	Hindu	125 (51.7)
	Muslim	65 (26.9)
Education[#]	Professional or Honors[a]	36 (14.9)
	Graduate or Postgraduate[b]	18 (7.4)
	Intermediate/Post-High School[c] diploma	97 (40.1)
	High School Certificate[d]	49 (20.2)
	Middle School Certificate[e]	42 (17.4)
	Primary School or Literate[f]	36 (14.9)
	Illiterate	18 (7.4)
Occupation[#]	Professional	5 (2.1)
	Semi-professional	7 (2.9)
	Clerical, Shop Owner, Farmer	11 (4.5)
	Skilled Worker	19 (7.9)
	Unskilled Worker	48 (19.8)
	Retired	17 (7.0)
	Unemployed	135 (55.8)
Marital status	Never married	3 (1.2)
	Currently married	214 (88.4)
	Divorced/Separated	3 (1.2)
	Widowed	22 (9.2)
Monthly income of family (¤)	≥100000	30 (12.4)
	50000-100000	12 (5.0)
	25000-50000	69 (28.5)
	<25000	131 (54.1)
Tobacco use	Yes	78 (32.2)
	No	164 (67.8)
Alcohol use	Yes	39 (16.1)
	No	203 (83.9)

Variables	Sub-categories	Number of patients (%) *n*=242
Self-reported physical activity	Yes	109 (45.0)
	No	133 (55.0)
Body mass index (BMI=Weight in kg divided by height in meters squared)	Underweight (< 18.5)	21 (8.7)
	Healthy weight (18.5-24.9)	135 (55.8)
	Overweight (25.0-29.9)	80 (33.1)
	Obese (30.0 and above)	6 (2.5)
Family history of cancer	Yes	109 (45.0)
	No	133 (55.0)
Type of cancer	Head-and-neck	56 (23.1)
	Gastrointestinal	45 (18.6)
	Breast	56 (23.1)
	Respiratory system	13 (5.4)
	Female reproductive system	27 (11.2)
	Prostate	7 (2.9)
	Blood and lymphatics	24 (9.9)
	Urinary system	4 (1.7)
	Others	10 (4.1)
Duration of treatment for cancer	< 1 month	103 (42.6)
	1-6 months	90 (37.2)
	6-12 months	49 (20.2)

[#]Based on the revised Kuppuswamy scale;

[a]Professional education like medicine (MBBS), engineering degrees (bachelor's degree in engineering or architecture);

[b]Bachelor's and master's degree in arts, science, and humanities;

[c]Class 12 with vocational diploma;

[d]Class 10 pass/Class 11 pass;

[e]Class 8 and 9 pass;

[f]Education up to 7th grade;

[g]Can only read but not write with understanding

Table 2
Distribution of comorbidities among patients with cancer

Variables	Sub-categories	Number of patients (%) *n*=242
Hypertension	Yes	82 (33.9)
	No	160 (66.1)
Onset of hypertension	Before the diagnosis of cancer	70 (85.3)
	After the diagnosis of cancer	12 (14.7)
Diabetes	Yes	53 (21.9)
	No	189 (78.1)
Onset of diabetes	Before the diagnosis of cancer	36 (67.9)
	After the diagnosis of cancer	17 (32.0)
Cardiovascular diseases (CVDs)	Yes	12 (5.0)
	No	230 (95.0)
Onset of CVD	Before the diagnosis of cancer	3 (25)
	After the diagnosis of cancer	9 (75)
Stroke	Yes	3 (1.2)
	No	239 (98.8)
Onset of stroke	Before the diagnosis of cancer	3 (100)
Respiratory disorder	Yes	22 (9.1)
	No	220 (90.9)
Onset of respiratory disorder	Before the diagnosis of cancer	22 (100)
Kidney disorder	Yes	15 (6.2)
	No	227 (93.8)
Onset of kidney disorder	Before the diagnosis of cancer	15 (100)
Liver disease	Yes	13 (5.4)
	No	229 (94.6)
Onset of liver disease	Before the diagnosis of cancer	13 (100)
Cognitive impairment	Yes	2 (0.8)
	No	240 (99.2)
Onset of cognitive impairment	Before the diagnosis of cancer	1 (50.0)
	After the diagnosis of cancer	1 (50.0)
Arthritis	Yes	57 (23.6)
	No	185 (76.4)
Onset of arthritis	Before the diagnosis of cancer	52 (91.2)
	After the diagnosis of cancer	5 (8.8)
Depression	Yes	21 (8.7)
	No	221 (91.3)
Onset of depression	Before the diagnosis of cancer	3 (14.2)
	After the diagnosis of cancer	18 (85.8)

Table 3
Correlates of comorbidities among patients with cancer

Variables	Yes (*n*=170), *n* (%)	No (*n*=72), *n* (%)	Adjusted Odds ratio (95% CI)	*P*
Age (in years)				
31-50	28 (16.5)	30 (41.7)	1	
51-70	142 (83.5)	42 (58.3)	5.962 (2.844-12.500)	<0.001*
Sex				
Male	70 (41.2)	24 (33.3)	1	0.108
Female	100 (58.8)	48 (66.7)	0.526 (0.240-1.151)	
Religion				
Hindu	95 (55.8)	30 (41.6)	1	0.312
Others$	75 (44.1)	42 (58.3)	0.707 (0.361-1.385)	
Family history of comorbidities				
Yes	123 (72.3)	38 (52.7)	1	<0.001*
No	47 (27.6)	34 (47.2)	0.234 (0.107-0.508)	
Body Mass Index (BMI)				
Normal weight and below	117 (68.8)	39 (54.2)	2.847 (1.260-6.432)	0.012
Overweight and above	53 (31.2)	33 (45.8)	Ref	
Treatment duration				
≤6 months	21 (12.4)	28 (38.9)	1	<0.001*
>6 months	147 (87.6)	44 (61.1)	4.058 (1.769-9.305)	

$Others includes Christians and Muslims,

*denotes statistically significant *P*