Epidemiology and Cost of Patients with Cancer in Iran: 2018

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Abstract

Background: Third leading cause of mortality in the world is cancer, with more than 12 million new cases and nearly 7.6 million deaths in 2007. The time estimation of healthcare costs of patients with cancer is an important component in developing national programs and policies of cancer. The present study aimed to investigate the epidemiology and costs of hospitalization of patients with cancer who were admitted to a regional referral center of the eastern Iran.

Methods: The present research was descriptive and had a cross-sectional and population-based design. It was conducted on all patients with cancer in a regional referral center in eastern Iran in 2018. The files of hospitalized cancer patients with disease codes of C0 to D48/9 and all patients who were admitted to the center for the treatment of cancer in 2018 and those who were discharged, were extracted and classified based on international codes of ICD10. Costs of the present study consisted of four categories including direct costs of cancer patients, direct costs of admission due to the cancer, direct outpatient costs, and indirect costs. Statistical data analysis was done by using criteria such as frequency, mean, and standard deviation through STATA Version 11.

Results: During the study, 1467 cancer patients were referred to Omid Hospital of Mashhad. Among them, 49.9% were males and 50.1% were females. 183 patients were in age range of 56-60 years. The highest prevalence and hospitalization were related to cancer of gastrointestinal organs (36%), and the highest hospital cost belonged to cancers involving bone, cartilage and joints (51.855 USD). The total cost of treating cancer patients was 1074990 USD and the average cost of cancer patients was 73278 USD per patient. Hoteling with a portion of 28% comprised the highest cost. The patients' share of out of pocket payment for treatment cost was 7% and the governmental share was 6%. The highest cost of treatment for cancer patients was paid by insurance companies (87%).

Discussion: The research results indicated that cancer patients bore high direct and indirect costs during their treatment; hence, new policies for reducing costs in these cases are needed. The increasing number of cancer patients and their treatment costs requires the active participation of all responsible organizations along with continuing financial support by financial institutions such as banks or charities and the development of appropriate government policies on supporting these patients.

Keywords: Epidemiology, Direct and indirect costs, Cancer

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Introduction

The third leading cause of mortality in the world is cancer, with more than 12 million new cases and nearly 7.6 million deaths in 2007.[1,2] It is expected that the number of new cases of cancer might increase from 10 million people in 2000 to 15 million people in 2020, and it is forecasted that a large number of these serious cases will occur in less developed regions of the world due to lack of various factors such as appropriate policies, effective monitoring and control of cancer, proper healthcare, financial resources, full national coverage and effective preventive policies.[3,4] Several factors play roles in increasing cancer in the world; and the rapid aging of the world's population is an important factor in increasing cancer worldwide. Diet, tobacco, other drugs and infectious factors are other factors contributing to cancer increase.[5] Cancer treatment usually includes frequent hospital admissions, the use of provided services by physicians and other clinical staff, such as use of laboratory and advanced diagnostic tests, chemotherapy, and expensive drugs. Moreover, surgery and radiotherapy are medical requirements of this disease in most cases. Cancer treatment also requires extensive outpatient visits.[6]

Direct healthcare costs constitute the first group of cancer patients' costs. These types of costs are related to the provision of inpatient and outpatient services for patients including costs that are provided by health centers (e.g. hospitals and outpatient clinics), personnel (physicians, nurses and other specialists), medical services, alternative and supplementary care, and any medication.[7,9] The second group includes indirect costs or lost productivity due to the absence from work, home and society because of illness and the premature death.[10, 11] These costs reduce the household income for many patients and their families. In this regard, self-employed patients can be severely affected.[12] Additional medical costs are other kinds of costs and include admission and outpatient costs associated with the diagnosis and treatment of non-cancer diseases that occur during an active cancer and are among direct costs.[13]

According to the American National Institutes of Health, cancers annually impose high costs to individuals and society. In 2008, 228 million USD per year was spent for treatment of patients and 40 percent of cost belonged to direct cost of treatment, 8% to indirect cost due to the loss of the of active workforce of society, its effect on the production and 52% to indirect cost due to the patient death and the patient loss in society.[14] The cancer treatment is very expensive, so that it can threaten the lives and well-being; moreover, it might threaten the financial security.[8,10] In fact, after the burden of human death, the economic dimension and imposed costs on individuals and society are the most important dimensions of cancer.[14] Time estimation for care costs of cancer patients is an important component in developing national programs and policies of cancer.[15] Studies on costs of a disease aim to find out the economic impact of a disease in the society (economic pressure). These descriptive studies seek to determine types and amounts of costs and problems in a healthcare system as an economic burden.[16] These studies can also determine a purposive framework of public policies for allocating public research budgets.[17,18] Information about costs of diseases such as cancer as well as analysis of costs allows managers and decision makers to make a fair comparison between different resource uses and provide a tool for tracking good work, measuring efficiency and predicting costs. In Iran, despite having recording measures for diagnosing or detecting various cancers in various provinces or the whole country, there is a little or no estimation of cancer patients and their costs. The present study was aimed to evaluate the epidemiology and treatment costs of cancer patients in east of Iran in 2018.

Materials and Methods

In this descriptive applied study, to estimate the economic burden imposed by cancer in 2018, the prevalence-based approach was used.

This cross-sectional and census study was conducted on all cancer patients in the Regional Referral Center of eastern Iran in 2018. In the

present study, costs of all cancers were evaluated. Cancer types were extracted and classified based on the international classification of diseases by the World Health Organization (WHO) edition 10 with disease codes of C0 to D48/9 and all patients who were admitted to and discharged from the center for treatment of cancer in 2018 (Table 1). Information on various cancers was separately documented.

By examining patients' files, the research group extracted and evaluated all cost data of patients admitted to Omid Hospital affiliated to Mashhad University of Medical Sciences. Medcare Information System (MES at: www.medcare.gov.com) was utilized to detect types

of cancer and ensure the accuracy of information. MES is a system under the supervision of the Ministry of Health of Iran for the registration and monitoring of patient information.

Outcomes of this study were: cancer type in terms of gender and in the largest age group, length of stay and costs of hospital based on types of cancer, cost distribution per cancer patient and ratio in cancer patients, outpatient costs, and indirect costs.

In the present study, costs included four types, namely direct costs of admitted cancer patients; outpatient costs and indirect costs. In order to calculate direct costs for admission of cancer patients and cancer diseases, all records in patients'
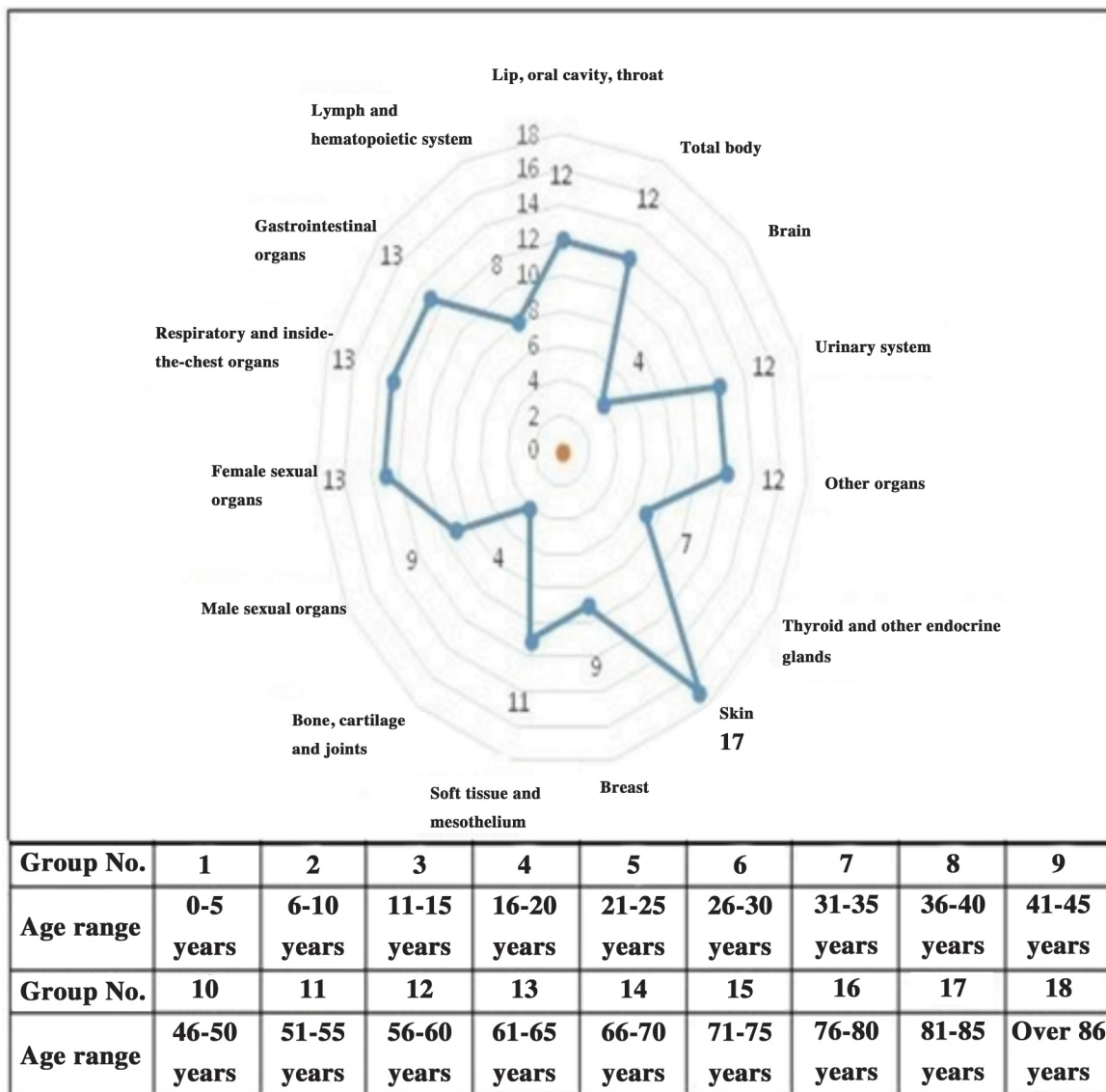

Group No.	1	2	3	4	5	6	7	8	9
Age range	0-5 years	6-10 years	11-15 years	16-20 years	21-25 years	26-30 years	31-35 years	36-40 years	41-45 years
Group No.	10	11	12	13	14	15	16	17	18
Age range	46-50 years	51-55 years	56-60 years	61-65 years	66-70 years	71-75 years	76-80 years	81-85 years	Over 86 years

Figure 1. Cancer type according to age group of the studied population.

Table 1. Cancer types based on ICD10

Type of cancer	Diagnosis code
Lip, oral cavity, throat	(C0-C14),D10,D37.0,D38.0
Lymph and hematopoietic system	(C81-C96),C77,D18,D45,D46
Gastrointestinal organs	(C15-C26),D00,D01,D12,D13,D37.1,D37.9
Respiratory and inside-the-chest organs	(C30-C39),C77,D2,D14,D15,(D38.1-D38.6)
Bone, cartilage and joints	C40,C41,D16
Female sexual organs	(C51-C58),D6,D7,D25,D28,D39
Male sexual organs	(C60-C63),D29,D40
Soft tissue and mesothelium	(C45-C49),D17,D19,D20,D21
Breast	C50,D5,D24
Skin	C43,C44,D3,D4,D22,D23
Thyroid and other endocrine glands	(C73-C75),D11,D34,D35,D44
Urinary system	(C64-C68),D30,D41
Brain	(C69-C72),D31,D33,D42,D43
Other organs	C76,C79,C80,D9,D36

files were considered including laboratory, anesthesia, operating room, surgeon fee, nursing service, medicines, consumables, hoteling, chemotherapy, pathology, medical visits, and other costs (e.g. counseling, physiotherapy, sonography, radiology, CT scan, radiography, echocardiogra-
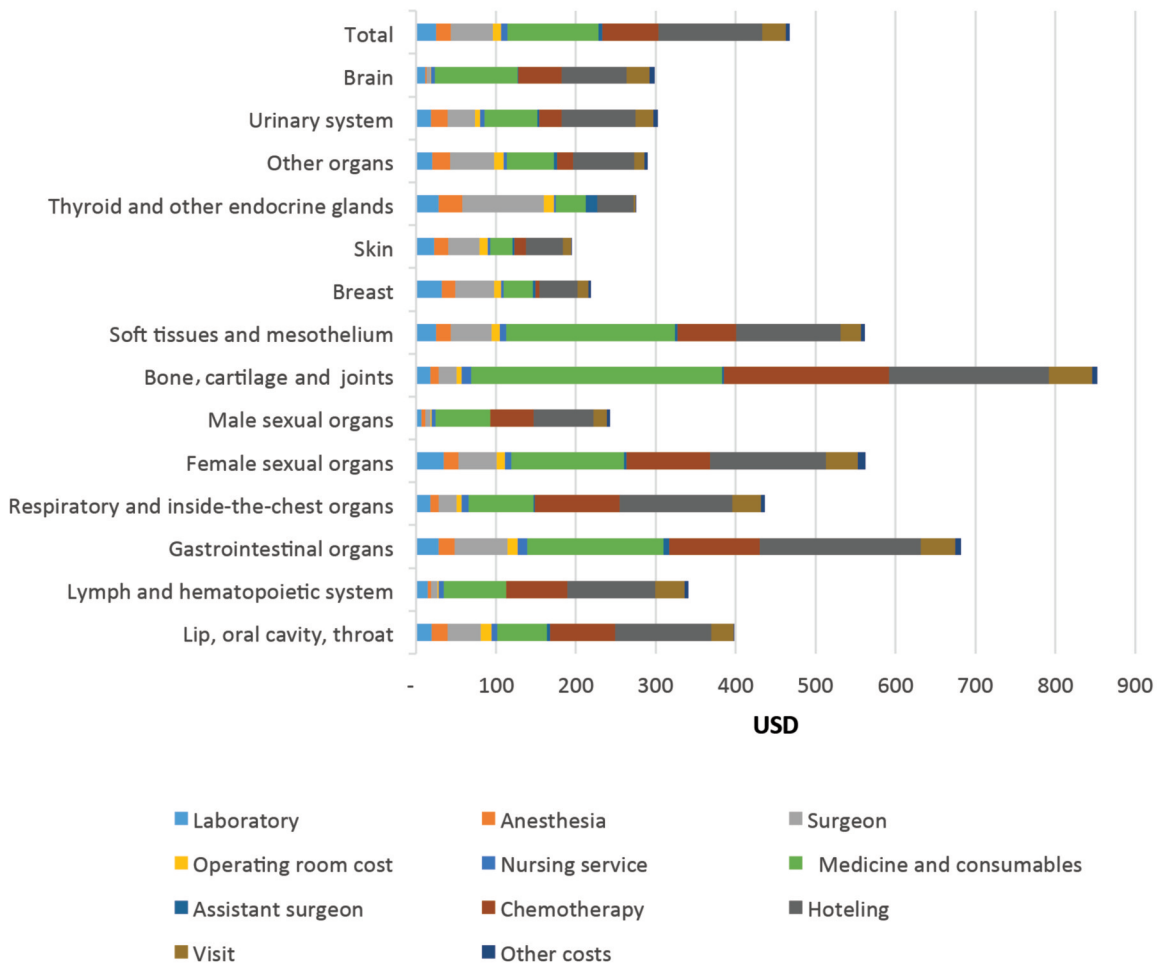
Figure 2. Cost distribution in USD per cancer patient.

Table 2. Cancer type in terms of gender in the studied population

| Type of cancer	Female		Male		Female and male	
	Number	Percentage	Number	Percentage	Number	Percentage
Lip, oral cavity, throat	20	3%	27	4%	47	3%
Lymph and hematopoietic system and other related tissues	33	4%	39	5%	72	5%
Gastrointestinal organs	196	26%	326	45%	522	36%
Respiratory and inside-the-chest organs	19	3%	45	6%	64	4%
Female sexual organs	65	9%	0	0%	65	4%
Male sexual organs	0	0%	24	3%	24	2%
Bone, cartilage and joints	14	2%	21	3%	35	2%
Soft tissues and mesothelium	33	4%	39	5%	72	5%
Breast	200	27%	1	0%	201	14%
Skin	12	2%	20	3%	32	2%
Thyroid and other endocrine glands	51	7%	17	2%	68	5%
Urinary system	8	1%	28	4%	36	2%
Brain	5	1%	9	1%	14	1%
Other organs	93	12%	122	17%	215	15%
Total	745	100%	722	100%	1467	100%

phy, and other medical procedures). The top-down costing was done if the detailed cost data was not recorded in a file. The researcher carried out top-down costing by allocating all costs to activities and experiments by using measured allocation criteria.

Furthermore, the cost data of outpatient patients was extracted by checking hospital accounting records.

Because the tariff of medical services is identical across Iran, the results from this center can be generalized to the whole country.[19]

In order to estimate the indirect costs, assuming that the monetary value of productivity lost due to morbidity or premature death caused by an illness equals the current wage, the human capital approach was used.[20] As breast cancer patients are usually able to perform their daily activities, the morbidity costs were not calculated for them.[21] The lost production was calculated due to the
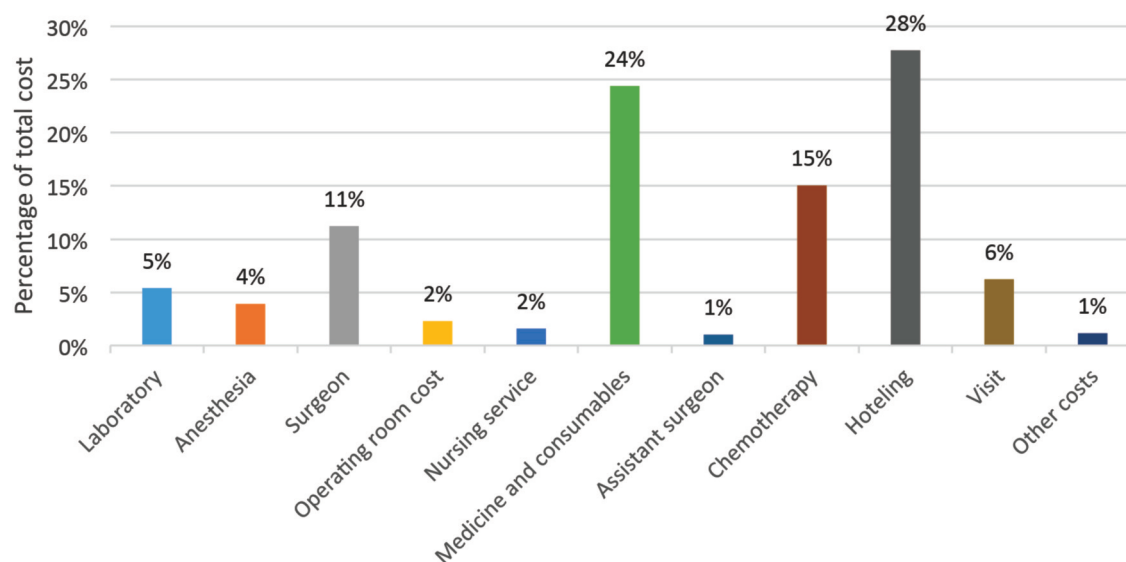
Figure 3. Cost distribution ratio in cancer patients.

Table 3. The length of stay and costs of hospital based on types of cancer

Type of cancer	Average hospital stay per visit	Number of patients	Number of patient referrals	Per capital cost	Share of patient cost payment		
					Insurance	Government	Patient
Lip, oral cavity, throat	5.2	47	106	399.26	89%	4%	7%
Lymph and hematopoietic system	4.8	72	191	346.32	89%	5%	5%
Gastrointestinal organs	9.1	522	1.523	686.99	88%	6%	7%
Respiratory and inside-the-chest organs	6.5	64	180	440.46	87%	7%	7%
Female sexual organs	6.1	65	175	566.06	87%	7%	5%
Male sexual organs	5.1	24	39	247.56	90%	5%	5%
Bone, cartilage and joints	5.5	35	133	855.51	89%	7%	4%
Soft tissues and mesothelium	5.7	72	169	563.43	89%	5%	5%
Breast	3.9	201	344	243.39	88%	5%	8%
Skin	3.9	32	45	197.4	85%	5%	10%
Thyroid and other endocrine glands	3.7	68	78	298.93	84%	5%	11%
Other organs	4.8	215	311	292.85	83%	8%	9%
Urinary system	4.8	36	83	324.1	89%	3%	8%
Brain	5.1	14	21	300.87	91%	5%	4%
Total	6.3	1.467	3.398	475.9	87%	6%	7%

patients' work absence in order to analyze indirect costs of treating patients; hence, number of lost days due to the hospitalization during 2018 was multiplied by the average daily income of each Iranian person. People aged 25 to 60 years were considered to calculate this type of cost.

Given the varying values of different currencies and the fact that price of a commodity varies according to economical conditions in different countries, a measurement that can be used to compare countries and different services is needed. In order to solve this problem according to the extracted statistics from the WHO and World Bank websites in 2011, a $ PPPUS was converted to Rial of Iran; and the figure was used to convert the Iranian Rial to $ PPPUS at all stages of estimates. (1 USD=Rial 100000)

Statistical data analysis was done by using criteria such as frequency, mean, standard deviation and allocation of indirect costs to different groups of diagnostic codes of cancer patients by using STATA Version 11.

This research was presented to the Ethics Committee of Mashhad University of Medical Sciences and approved (IR.MUMS.REC.1396.207 Code of Ethics). This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Results

The present research investigated 1467 cancer patients among whom 49.3% were male and 50.7% were female. The highest number of patients was in the age range of 56-60 years (Figure 1). Furthermore, nearly 99% of patients had basic insurance. Since 2014 and by implementing the health system evolution program (the program aims to improve Iran's health systems with three approaches to protect people from the public, create equity in access to health services, and improve service quality), the patients have received the health subsidy that decreases the out-of-pocket payment by admitted patients (10% in patients with urban insurance, and 5% in patients with rural insurance). According to the line of credit 30303, which is funded by the Ministry of Health, cancer patients receive financial discount; in addition, charities or hospitals provide some portions of the costs. In the present study, for all cancer patients (with and without insurance) the share of out-of-pocket payment by patients was 7%, and the government's share including health subsidies, discounts, and lines of credit was 6%. The highest cost of treatment for cancer patients was paid by insurance companies (87%).

The most common type of cancer was seen in gastrointestinal organs in males (326 patients)

Table 4. Costs of outpatient services for studied cancer patients

Outpatient services	Number of patients	Number of visits	Patient share of hospital cost		Total cost	Cost per patient
			Insurance	Patient		
Cancer patients	1467	39829	94.5%	5.5%	363450	247.75

*All costs are in USD

and breast cancer in females (200 patients). In total, the cancer of gastrointestinal organs was the most common type of cancer with prevalence of 36% (522 patients) of the total cancer patients (Table 2).

The highest incidence of cancer was observed in the age group of 56 to 60 years. The most common types of cancer in the age range of 61 to 65 years were cancers of gastrointestinal organs, respiratory organs, and female sexual organs.

The average length of stay in the hospital was 6.3 days per visit. According to diagnostic codes of cancer patients referring to hospital, they were classified into 14 groups in terms of organs with cancer (Table 3). The maximum length of hospital stay per visit (4.3 days) was related to gastrointestinal organs and then soft tissues and brain (9.1 days).

The average cost of cancer patients was 475.9 USD per patient and the highest cost belonged to the bone, cartilage and joints group (855.51 USD).

The patients' share of cost was higher than other types of cancers, in cancers of skin, thyroid and other endocrine glands, and other organs.

The report of cancer patients admitted to hospitals consisted of 11 items. Figure 2 presents their USD figures per patient.

The main cost items for cancer patients belonged to drug and consumables (24% of total costs), hoteling (28%), and chemotherapy (15%). (Figure 3)

Based on results, the first direct cost (cancer patient admission) was 444150 USD and the second direct additional cost (cost of cancer patients' referrals due to cancer-related diseases) was 253990 USD.

Based on table 4, the third type of direct cost was related to outpatient services, and it was 247.75 USD per patient and a total cost of 36345 USD per patient.

Indirect costs constitute the fourth type of cost.

For measuring indirect costs, the mean time of absence from work was 26.5 days. Since the mean daily wage for employed and unemployed was 1.96 USD and 0.8 USD (from the website of The Central Bank of the Islamic Republic of Iran); therefore, the lost production due to the absence from work was 90420 USD (Table 5).

In the present study, the total cost of cancer patients was 1074990 USD per year (Table 6).

Discussion

The present study aimed to evaluate the epidemiology and costs of cancer patients in east of Iran in 2018. In this research, the highest prevalent types of cancer were observed in the age group of 56-60 years. In a study in Kerman, Iran, people over 60-64 years of age had the highest percentage (11.60%) of the total incidence of cancer.[22] This findings suggested that aging population was an important factor in increasing the frequency of cancer. In the present study, the most common type of cancer occurred in gastrointestinal organs among males and breast cancer in females. According to studies from 2004 to 2009, the most common types of cancer were gastrointestinal cancer in males and breast cancer in females in Iran.[23] According to results, breast cancer accounted for 27% of total cancers among the Iranian women and was the most common cancer among women.[24] The age of women with cancer was approximately 41-45 years according to findings of studies in Iran. This range of age was about 10 years younger than the western countries.[25,26] Probably this is due to the younger population structure of Iran than the western countries.[27] Given the fact that women play significant roles in family and society in the fourth decade of life, the low age of patients imposes direct costs on patients or insurance organization in addition to loss of life and inability of engaging in social activities compared to older patients.

Table 5. Indirect cost for studied cancer patients

Status	Number of patients	Mean of missed work days	Total of missed work days	Mean cost per days	Total cost
Employed patient	918	26.5	24327	1.96	47.681
Unemployed patient	549	26.5	14548.5	0.8	11.639
Patient's accompany	1467	26.5	38875.5	0.8	31.100
Total					90.420

*All costs are in USD

In the present study, cancer of gastrointestinal organs was the most common type of cancer among males (46%) and it was the most common type of cancer with the prevalence of 36% on the whole. In a worldwide study, gastrointestinal cancer was found to be the highest one in Asia and South America.[28] The maximum length of hospital stay per visit (4.3 days) was also related to the cancer of gastrointestinal organs. Screening gastrointestinal cancers is now problematic and costly. Therefore, the primary prevention approach is preferable to therapeutic interventions to control the disease.[29-32] In the present study, the average cost of cancer patients was 475.9 (USD) per patient. This amount is much less than costs of cancer in other countries.[33,34.]This difference in costs may be because of the health sector finance paying in Iran, low costs of treatment, and non-prescription of expensive drugs in Iran compared to other countries. It is also difficult to compare cost assessment studies due to the application of different methods for calculating treatment costs that depend on the type and purpose of study and available data. In the present study, the highest cost of 855.51 USD belonged to bone, cartilage and joint cancers. In a conducted study in the European Union, the greatest cost of cancer was related to lung cancers,[35] which was inconsistent with results of the present study. The main cost items for cancer patients were related to medicine and consumables (24% of total cost), hoteling (28%), and chemotherapy (15%). In a study by Gordon et al., the cost of medicine, with an average of 824 USD, was considered to be the most costly.[36] In a study in Turkey, chemotherapy was a main cost item for cancer patients.[13] Therefore, new policies should be adopted to reduce costs in these cases. According to results of the present study, hospitalization costs (39%), direct costs of cancer (22%), outpatient services (32%), and indirect costs (due to the job loss) (8%) accounted for the total cost of cancer. In another study done in Turkey, direct costs (41%) and indirect costs (resulting from job loss and early death) (59%) accounted for the total cost.[13] This difference is due to the lack of access to data on mortality in the present study, and failure to calculate the lost cost because of the early death from the illness in the present study.

Conclusion

Given that the tariffs for medical treatment are the same in all Iranian hospitals, this information can be generalized to the whole country. The research results indicated that patients with cancer faced high direct and indirect costs during their treatment. This trend is likely to continue in the near future. Drugs and consumables, hoteling, and chemotherapy imposed higher costs on patients. Therefore, new policies should be adopted to reduce costs in these cases; for instance, to reduce the length of treatment in hospitals. Studies should be conducted on the cost-effectiveness of identifying alternative

Table 6. Total cost for studied cancer patients

Admission of cancer patient	Admission of patients with cancer-related diseases	Outpatient services	Indirect costs	Total costs	Cost per patient
444150(39%)	253990(22%)	363450(32%)	90420(8%)	1152010(100%)	785

Note: All costs are in USD.

drugs and consumables and equipment at a lower cost and higher effectiveness to remove financial barriers for patients; thus, cancer patients will not delay their treatment for high costs and can manage their illnesses better. Due to the high share of insurance companies in paying for cancer patients, these companies need to invest in preventive programs. The insurance companies should invest in preventing, screening, informing, and in particular building the culture of avoiding the underlying causes of cancer to reduce high costs of treatment by reducing the number of cancer patients. The increasing number of cancer patients and costs of their treatment need the active participation of all responsible organizations along with continuing financial support by financial institutions such as banks or charities and developing appropriate government policies on supporting these patients. In order to understand trends and costs of cancer better, it is recommended to perform similar studies in other regions of Iran.

References

1. Featherstone H, Whitham L. The cost of cancer. Policy Exchange: London; 2010.p.56-77.
2. Thun MJ, DeLancey JO, Center MM, Jemal A, Ward EM. The global burden of cancer: priorities for prevention. *Carcinogenesis*. 2010;31(1):100-10. doi: 10.1093/carcin/bgp263.
3. Salminen E, Izewska J, Andreo P. IAEA's role in the global management of cancer-focus on upgrading radiotherapy services. *Acta Oncol*. 2005;44(8):816-24.
4. Kanavos P. The rising burden of cancer in the developing world. *Ann Oncol*. 2006;17(8): 15-23. doi: 10.1093/annonc/mdl983.
5. Stewart B, Kleihues P. World Cancer Report. Lyon, France: Internat. Agency Res. on Cancer Press; 2003.
6. Barr RD, Feeny D, Furlong W. Economic evaluation of treatments for cancer in childhood. *Eur J Cancer*. 2004;40(9):1335-45. doi: 10.1016/j.ejca.2004.01.033.
7. Kim P. Cost of cancer care: the patient perspective. *J Clin Oncol*. 2007;25(2):228-32. doi: 10.1200/JCO.2006.07.9111.
8. Longo C, Deber R, Fitch M, Williams A, D'souza D. An examination of cancer patients' monthly 'out−of−pocket' costs in Ontario, Canada. *Eur J Cancer Care (Engl)*. 2007;16(6):500-7. doi:10.1111/j.1365-2354.2007.00783.x.
9. Hayman JA, Langa KM. Estimating the costs of caring for the older breast cancer patient. *Crit Rev Oncol Hematol*. 2003;46(3):255-60. Doi:10.1016/S1040-8428(03)00025-8.
10. Longo CJ. Characteristics of cancer patients' out-of-pocket costs in Ontario. *J Clin Oncol*. 2005; 22(14_suppl):8251. doi:10.1200/jco.2004.22.90140.8251.
11. Reeder CE, Gordon D. Managing oncology costs. *Am J Manag Care*. 2006;12(1):p3.
12. Sharp L, Timmons A. The financial impact of a cancer diagnosis. Ireland: National Cancer Registry Ireland; 2010. 129 p. Available from: http://hdl.handle.net/10147/316722.
13. Cakir Edis E, Karlikaya C. The cost of lung cancer in Turkey. *Tuberk Toraks*. 2007;55(1):51-8.
14. Siegel R, Cokkinides V, Jemal A. Cancer facts and figures for Hispanics/Latinos 2009-2011. Atlanta: AC Society. American Cancer Society; 2009.p.1-35.
15. Yabroff KR, Lamont EB, Mariotto A, Warren JL, Topor M, Meekins A, et al. Cost of care for elderly cancer patients in the United States. *J Natl Cancer Inst*. 2008;100(9):630-41. doi: 10.1093/jnci/djn103.
16. Jefferson T, Demicheli V, Mugford M. Elementary economic evaluation in health care. 2nd edition. London: BMJ Books, 2000. p.11-115.
17. Gross CP, Anderson GF, Powe NR. The relation between funding by the National Institutes of Health and the burden of disease. *N Engl J Med*. 1999;340(24):1881-7.doi: 10.1056/NEJM199906173402406.
18. Cooksey D. A review of UK health research funding: The Stationery Office; 2006.p.8-325.
19. Daroudi R, Sari AA, Nahvijou A, Kalaghchi B, Najafi M, Zendehdel K. The economic burden of breast cancer in Iran. *Iran J Public Health*. 2015;44(9):1225.
20. Schottenfeld D, Fraumeni JF. Cancer epidemiology and prevention; Economic impact of cancer in the United States. 3th ed. United States of America: Oxford University Press; 2006.p.202-214.
21. Max W, Sung H-Y, Stark B. The economic burden of breast cancer in California. *Breast Cancer Res Treat*. 2009;116(1):201-7. doi: 10.1158/1055-9965.EPI-11-0650.
22. Keyghobadi N, Rafiemanesh H, Mohammadian-Hafshejani A, Enayatrad M, Salehiniya H. Epidemiology and trend of cancers in the province of Kerman: southeast of Iran. *Asian Pac J Cancer Prev*. 2015;16(4):1409-13. doi:10.7314/apjcp.2015.16.4.1409.
23. Enayatrad M, Mirzaei M, Salehiniya H, Reza M. Trends in incidence of common cancers in Iran. *Asian Pac J Cancer Prev*. 2016;20-5.doi: 10.7314/apjcp.2016.17.s3.39.
24. Formenti SC, Arslan AA, Love SM. Global breast cancer: the lessons to bring home. *Int J Breast Cancer*. 2012:249501. doi: 10.1155/2012/249501.
25. Harirchi I, Ebrahimi M, Zamani N, Jarvandi S,

Montazeri A. Breast cancer in Iran: a review of 903 case records. *Public Health*. 2000;114(2):143-5. doi:10.1038/sj.ph.1900623.

26. Mousavi SM, Montazeri A, Mohagheghi MA, Jarrahi AM, Harirchi I, Najafi M, et al. Breast cancer in Iran: an epidemiological review. *Breast J.* 2007;13(4):383-91.

27. Demographic Indicators [Internet]. Iranian Statistical Centre. 2011 [cited July 2011]. Available from: http://www.amar.org.ir/.

28. Rastogi T, Hildesheim A, Sinha R. Opportunities for cancer epidemiology in developing countries. *Nat Rev Cancer.* 2004;4(11):p909. doi: 10.1038/nrc1475.

29. Lygidakis NJ. Total gastrectomy for gastric carcinoma: a retrospective study of different procedures and assessment of a new technique of gastric reconstruction. *Br J Surg*. 1981;68(9):649-55. doi:10.1002/bjs. 1800680913.

30. Heptner G, Domschke S, Domschke W. The role of tumor markers in the diagnosis and management of gastrointestinal cancer. *Hepatogastroenterology.* 1986;33(4):140-4.

31. Janssen JC, Maartmann-Moe H, Lie RT. Concentrations of serum proteins and erythrocyte sedimentation rate in patients with different histological types of gastric carcinoma. *Eur J Surg Oncol.* 1987 Jun;13(3):207-11.

32. Lipkin M. Biomarkers of increased susceptibility to gastrointestinal cancer: new application to studies of cancer prevention in human subjects. *Cancer Res.* 1988;48(2):235-45.

33. Barron JJ, Quimbo R, Nikam PT, Amonkar MM. Assessing the economic burden of breast cancer in a US managed care population. *Breast Cancer Res Treat.* 2008;109(2):367-77. doi:10.1007/s10549-007-9650-4.

34. Dahlberg L, Lundkvist J, Lindman H. Health care costs for treatment of disseminated breast cancer. *Eur J Cancer.* 2009;45(11):1987-91. doi:10.1016/j.ejca. 2009.03.023.

35. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol*. 2013;14(12):1165-74. doi: 10.1016/S1470-2045(13)70442-X.

36. Gordon LG, Ferguson M, Chambers SK, Dunn J. Fuel, beds, meals and meds: out-of-pocket expenses for patients with cancer in rural Queensland. *Cancer Forum.* 2009; 33(3).