

History of Medicine in Iran

Medical Oncology, History and Its Future in Iran

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Abstract

Systemic therapy is one of the cornerstones of cancer treatment. In 1972, following representations by American Society of Clinical Oncology (ASCO), the American Board of Internal Medicine (ABIM) recognized medical oncology as a new subspecialty of internal medicine. Subspecialty of Hematology and Medical Oncology was emerged in Iran in 1983.

In the past, modern medical treatments and education were started in Dar Al-fonun school and then in Tehran University; now six universities in Iran are training in Subspecialty of Hematology and Medical Oncology. There are also ten active hematopoietic stem cell transplantation centers, thirty-one provincial medical schools, use their specialized services. Future goals for Hematology and Medical Oncology in Iran include expansion and reinforcement of multidisciplinary teams across the country, early detection and prevention of cancer, providing educational program and conducting cancer researches. To achieve these goals, it is necessary to establish Cancer Hospitals in each province that link together through a network.

Keywords: Cancer, history, Iran, medical oncology

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Introduction

Surgery has been the oldest method of treatment of solid tumors such as breast cancer or gastric cancer. Today, surgery continues to be the major therapeutic approach to solid tumors in most parts of the body. However, the local recurrence or distant metastasis has remained the main cause of death in cancer patients. Radiation therapy was often used after surgery, reduced the risk of local recurrence and metastasis, and improved the survival rates to approximately 33% in cancer patients.¹ The reason for relapse is thought to be the presence of micrometastases in other organs that later leads to treatment failure and death. Cancer is a systemic disease, even it is apparently localized in a specific organ.² In the past, attempts to treat hematologic malignancies have led in disappointing results and patient's death after the natural progression of the disease.

Now the treatment of cancer is divided into local therapies (sur-

gery and radiation therapy) and systemic therapies (chemotherapy, hormone therapy, immunotherapy, targeted therapy and hematopoietic stem cell transplantation). It is now recognized that, a multidisciplinary team (MTD) for optimal treatment of cancer is essential. The presence of three main bases (surgery, radiation therapy and medical oncology) of the team is mandatory for cancer treatment.

Chemotherapy

An accidental release of Sulfur mustard from an Italian warship during World War I led to the observation that both bone marrow and lymph nodes were markedly depleted in those men, who were exposed to the mustard gas.³ In 1919, Krumbhaar, et al. reported that 23 of 108 soldiers who had been exposed to the yellow cross gas, had developed leukopenia, showing a direct relationship between the severity of leukopenia and prognosis.⁴ After these reports, many research studies were conducted, leading to the discovery of the first chemotherapeutic agent.

In 1943, two pharmacologists (Louis Goodman and Alfred Gilman) at Yale University, administered nitrogen mustard to a patient with severe airway obstruction and refractory non-Hodgkin's lymphoma to radiation therapy. This was the beginning of the modern chemotherapy in human.^{1,5-8}

Birth of Medical Oncology

According to Vincent DeVita, the field of medical oncology did not officially exist as a subspecialty of internal medicine in the 1960s. Chemotherapy was conducted by non-qualified staff in treatment centers that led to serious systemic side effects and internal organ damages; especially the bone marrow, liver, kidney and heart and no survival benefit was found. In 1972, following representations by ASCO, the American Board of Internal Medicine (ABIM) recognized medical oncology as a new subspecialty

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of internal medicine.^{1,9}

Educational curriculum in Medical Oncology

The new curriculum^{10,11} in medical oncology created by ASCO in 1998 included basic scientific principles; principles in the management and treatment of malignant diseases; management and treatment of individual cancers; bone marrow transplantation; psychosocial aspects of cancer; supportive care; patient education; palliative care; bioethics, legal and economic issues; chemoprevention; procedures; screening and clinical experiences.

Hematology and Medical Oncology in Iran

Dual training in Hematology and Medical Oncology is being conducted in many training centers worldwide, because they share a common history and reflect fundamental overlaps.

The field of hematology covers a wide spectrum of disorders, including benign hematologic disorders, malignant hematologic disorders and stem cell transplantation. Medical oncology covers solid tumors, hematologic malignancies and stem cell transplantation (Figure 1). There is a three year program for dual certification in Hematology and Medical Oncology, while the duration of training in either subspecialty is 24 months, after receiving board certification in Internal Medicine.¹²⁻²⁰

The first articles published on cancer treatment date back to 2000 BC. Plant-derived anti-cancer drugs (containing compounds such as Copper, Sulfur, Arsenic and Mercury) as well as animal-derived ingredients (liver, bones and urine) were the most common therapies in cancer treatment.²¹

Majusi Ahvazi (10th century C.E.) in his book entitled “Teb Maleki” described the cancer as a hard lump, which is rarely treated with medications and should be removed by surgical knife.²² Razi (862 – 925 C.E) wrote about cancer and its treatment in his book known as Al-Hawi. In another work, Cannon of Medicine, Avicenna (980 – 1037 C.E) described different types of cancer, including nasal, eye, and tongue, uterine, liver and esophageal. Avicenna believed that the incidence of cancer was more common in autumn due to an excess of humors.^{22,23} The four Persian medical works on cancer are “Al-Hawi”, “Qanun fi Tibb”, “ Makhzan-o-al-advieh” and “Ekhtiyarat-e Badi”. These books are about anticancer medications that are mostly herbal with a few of animal and mineral origin.²⁴

Tehran University of Medical Sciences

Dar Al-Fonun school (Figure 2) that established in 1851 was the first modern institution of higher education, in which several books were translated from European resources and published in Iran. Then, the mission of medical education was taken over by Tehran University of Medical Sciences founded in 1934.²² Herbal

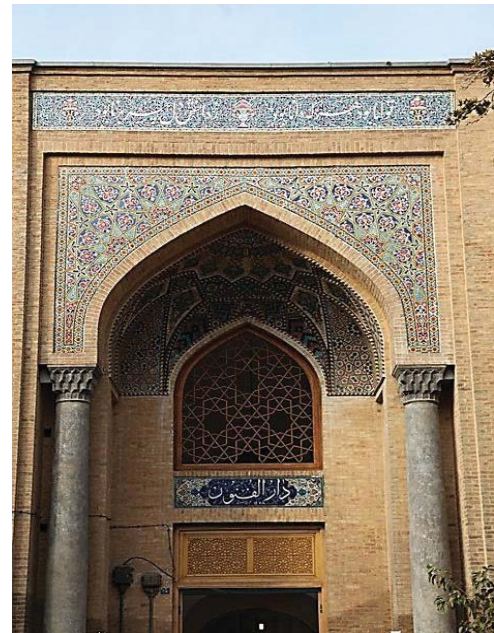


Figure 2. Dar al-Fonun school, modern science training in Iran, since 1851, Tehran



Figure 3. Dr. Yahya Pouya, founder the first Hematology and oncology ward in 1955 in Imam Khomeini Hospital Complex, Tehran University of Medical Sciences.²⁵

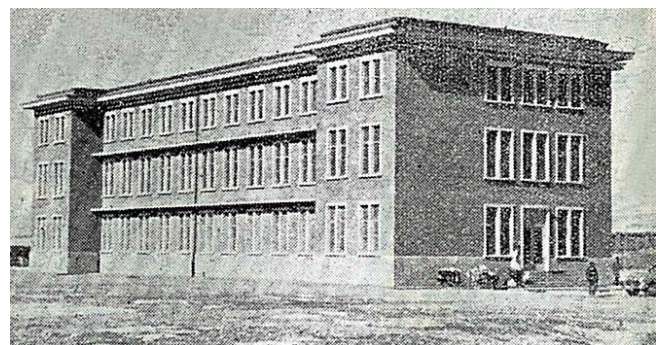


Figure 4. Infectious diseases ward in Imam Khomeini Hospital (Former Pahlavi Hospital) in 1955, Tehran University of Medical Sciences.²⁵



Figure 1. Training content relationship between hematology and medical oncology.¹²⁻²⁰

medicines have a vital role in both of traditional Iranian and modern medicine. In 1955, Dr. Yahya Pouya (Figure 3), a graduate of France's university, founded the first Hematology ward containing 20 beds in Imam Khomeini Hospital (Pahlavi) affiliated with Tehran University of Medical Sciences.

These Hematologic beds were first located in the infectious diseases ward (Figure 4). Acute leukemia was treated mostly with glucocorticoids and some few available chemotherapeutic agents at that time. In 1959, Hematology and Medical Oncology ward transferred to the Razi Hospital, and in 1970 was transferred to the Cancer Institute (Figure 5) of Imam Khomeini (Pahlavi) Hospital complex. In 1975, patients with hematologic malignancies were referred to Vali-e-Asr Hospital (Doctor Eghbal) for treatment, but solid tumor chemotherapy was still performed at the Cancer Institute. In 1986, the name of the chemotherapy ward in the Cancer Institute was changed to Medical Oncology Ward, consisting of 80 beds for systemic treatment of cancer patients.²⁵

Over the past few years, radiology and radiation therapy were united under the same discipline of radiology. In 1956, the division of diagnostic radiology was established at the Cancer Institute. After a couple of years, the first radiation therapy ward came into function in Iran.¹¹ The surgical ward of Cancer Institute was also founded in 1957. In 1956, research center and pathology laboratory were established at the Cancer Institute for cell-culture experiments and experimental production of cancers in animals.¹¹ In this year an electron microscope was also launched (Figure 6). Therefore, holistic care is delivered in a multidisciplinary approach to cancer treatment.

In 1990, the first bone marrow transplantation ward was established by Dr. Ardeshir Ghavamzadeh (Figure 7) in Shariati Hospital, affiliated with Tehran University of Medical Sciences. It is now expanded to one of the most prominent stem cell transplantation centers in the world with more than 300 successful transplants annually. A total of 4568 patients with hematologic disorders, solid tumors, genetic disorders and immune deficiency diseases have received transplantation in this center up to 2014 (Figure 8).

Bone marrow transplantation Centers in Iran

Now, we have ten active bone marrow transplantation centers in Iran including: 1) Shariati hospital, Tehran University of Medical Sciences; 2) Namazi hospital, Shiraz University of Medical Sciences; 3) Imam Khomeini hospital, Tehran University of Medical Sciences; 4) Taleghani hospital, Shahid Beheshti University of Medical Sciences; 5) Afzalipour hospital, Kerman University

of Medical Sciences; 6) Shafizadeh hospital Amirkola, Babol University of Medical Sciences; 7) MAHAK hospital, society to support children suffering cancer, Tehran; 8) Imam Reza hospital, Kermanshah University of Medical Sciences; 9) Shahid Ghazi Tabatabaee hospital, Tabriz University of Medical Sciences; and 10) Shafa hospital, Ahvaz Jundishapur University of Medical Sciences.

ISCDP (Iranian Stem Cell Donor Program)

More than half of the allogeneic transplants use unrelated donor products. Sixty-six unrelated volunteer donor registries from 47 countries and 44 cord blood banks from 29 countries are now listed on Bone Marrow Donors Worldwide (BMDW). Hematopoietic Stem Cell Transplantation (HSCT) has been performed in the Eastern Mediterranean and Middle East countries over the years and has shown qualitative and quantitative evolution in these regions; however, in contrast to developed countries, HSCT from matched unrelated donors has not improved in developing states. In view of the notable decrease in the family size in recent years, the creation of such unrelated donor banks seems to be essential to overcome this problem.

Due to the lack of unrelated donor banks in Iran and the Eastern Mediterranean countries, the Hematology-Oncology and the SCT research center in Iran submitted the unrelated bone marrow registry program to Tehran University of Medical Sciences in 2009. More than 23012 volunteers have now registered with this program and the chances of finding a match for patients have increased substantially (Figure 8).

ISCDP joined BMDW as the first HLA registry in Eastern Mediterranean and Middle East on March 8, 2011 and now there is an opportunity to search information for accredited donors listed on BMDW.

Shahid Beheshti University of Medical Sciences

Dr. Davoud Monadzadeh, a graduate from Chicago University, founded the Hematology and Medical Oncology ward at Shahid Modarres Hospital in 1978.

Dr. Mohammadali Varghaee, U.S. graduate in the subspecialty of Hematology and Medical Oncology, opened the Hematology and Medical Oncology ward at Taleghani Hospital in 1981. Hematology and Medical Oncology fellows are currently being trained at the hospital consisted of two discrete Hematology and Medical Oncology wards, containing 30 beds.

HSCT ward in Taleghani Hospital was inaugurated in 2007. By



Figure 5. Cancer Institute in 1956, Tehran University of Medical Sciences.²⁵



Figure 6. First Electron microscope in Iran, Cancer Institute in 1956, Tehran University of Medical Sciences.²⁵

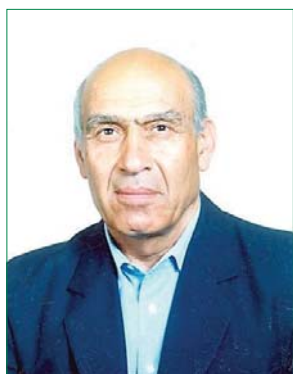


Figure 7. Dr. Ardeshir Ghavamzadeh, Faculty of Tehran University of Medical Sciences, Shariati hospital, founder of Hematopoietic stem cell transplantation (HSCT) and Medical Oncology in Iran



Figure 8. Hematology and Medical Oncology, HSCT research and ISCDP center, Shariati Hospital since 1999, Tehran University of Medical Sciences [from archive of the center with permission]



Figure 9. Emam Reza Hospital in Mashhad since 1934, Mashhad University of Medical Sciences [from public relations of the hospital]

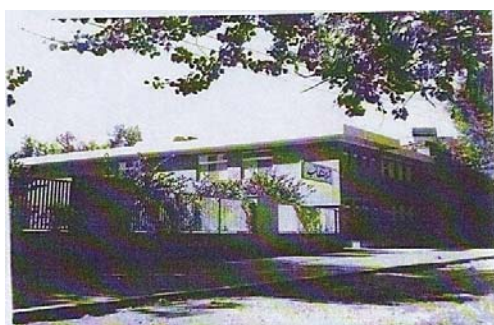


Figure 10. Omid hospice in Isfahan in 1971 [from public relations of the hospital]

the end of the September 2014, 417 autologous and allogeneic transplantations have been performed.

Mashhad University of Medical Sciences

In 1966, Abdol Hossein Afkari MD, a graduate of France's university established a separate discipline in Hematology and Medical Oncology at Mashhad University of Medical Sciences. For the first time, he inaugurated an eight-bed hematology ward at Shah Reza Hospital (previous name of Imam Reza Hospital) (Figure 9), but then was transferred to Ghaem Hospital.

Dr. Manouchehr Lari, a board-certified internist with subspecialty certification in Hematology and Medical Oncology from the University of Texas MD, Anderson Cancer Center, was hired in 1973 as an Assistant Professor at Ghaem Hospital affiliated with Mashhad University of Medical Sciences to train student and treat patients.

At present, there are 20 outpatient chemotherapy beds and 20 inpatient beds in the hematology and medical oncology ward of Imam Reza Hospital to provide treatment services. Ghaem Hospital has also 20 inpatient beds and 18 outpatient chemotherapy beds for treatment of patients with hematologic disorders. Moreover, the Isar Treatment Center is another outpatient clinic that provides services to patients.

Iran University of Medical Sciences

Dr. Azizalah Karamlou who had received his subspecialty certification in medical oncology from the United States served on the faculty from 1971 – 1983 at the Firoozgar Hospital. Ahmad Azizi served as MD professor of hematology and medical oncology at the Firoozgar Hospital from 1972 to 1997. Now Firoozgar Hospital consists of a 6-story building, providing therapeutic and educational services as well as palliative care to patients.

Ali Golshaeian, MD board certified hematologist and medical oncologist from French universities, was an attending physician at Shohadaye Hafte-Tir Hospital from 1985 to 2000. In 1999, the Division of Hematology and Oncology was opened at Rasool-e-Akram Medical Complex, consisting of several great hospitals. Dr. Vahid Moazed was an attending physician in the Division of Hematology and Oncology from 1984 to 1999.

Isfahan University of Medical Sciences

Omid hospice (Figure 10), the first center for treatment of cancer patients, was founded in 1971 by the benefactors of Isfahan and with the support of late Dr. Morteza Hakami.

In 1979, Jamshid Saranj (Figure 11), MD, German board-certified in the subspecialty of hematology and medical oncology opened the first Hematology and Medical Oncology Unit in Omid hospice.

At the present time, Seyed-Al shohada Hospital with a capacity of 46 beds in the oncology wards provides a wide range of services to cancer patients through multi-disciplinary teams (MDTs). In addition, Hematology and Medical Oncology resident Training Program is offered at this hospital.

Tabriz University of Medical Sciences

Azizalah Karamlou, who had graduated from U.S. Medical School, opened the division of Hematology (malignant and non-malignant hematologic disorders) at Tabriz University in 1967.

Jalil Vaez Maleki (Figure 12) has been on the hematology and



Figure 11. Dr. Jamshid Saranj, Faculty of Isfahan University of Medical Sciences, pioneer in Hematology and Medical Oncology in Isfahan



Figure 12. Dr. Jalil Vaez Maleki, Faculty of Tabriz University of Medical Sciences, Ghazi Tabatabaee Hospital, one of the pioneer in Hematology and Medical Oncology in Tabriz



Figure 13. Dr. Mansour Haghshenas (1937 – 2015), Faculty of Shiraz University of Medical Sciences, Namazi hospital, pioneer in Hematology and founder of the Medical Oncology Department in Shiraz



Figure 14. Dr. Nasrollah Sayyar, Faculty of Tehran University of Medical Sciences, Imam Khomeini Hospital Complex, one of the pioneers and first members of the Subspecialty Board of Hematology and Medical Oncology in Iran

oncology faculty since 1972 and actively involved in the treatment of patients in Tabriz.

In 1977, Hasan Samadi Damirchi Lou who had received subspecialty certification in hematology from the United States started his career at Tabriz University.

Iraj Asvadi Kermani, MD, hematologist and medical oncologist from Tehran University of Medical Sciences, along with Jalil Vaez, MD, hematologist and medical oncologist, opened a 104-bed Shahid Ghazi Tabatabaee Hospital in 1988, focusing solely on hematologic and oncologic disorders. It is the first single-specialty hospital containing an outpatient clinic, modern research laboratory, blood bank, general surgical ward and drugstore.

The Hematology and Medical Oncology residency Program was designed in 1984 to recruit 12 residents annually. In 2006, the Hematology and oncology Research Center affiliated with Tabriz University of Medical Sciences came into operation in the hematology and medical oncology unit. The Hematopoietic Stem Cell Transplantation (HSCT) Research Center affiliated with Tabriz University of Medical Sciences was also founded in 2014.

Shiraz University of Medical Sciences

Division of Hematology and Oncology initiated educational activities and research programs in 1971 under the direction of Dr. Nasr and Dr. Esmael Beigi. Four faculty members including: Dr. Mansour Haghshenas (Figure 13), Dr. Esmael Beigi, Dr. Jahangir Raafat and Dr. Mojab were recruited in Department of Hematology and Oncology to develop educational, research and treatment programs from 1971 to 1980. But in 1981, only Dr. Haghshenas remained at his position at Shiraz University of Medical Sciences.

Professor Mansour Haghshenas (1937 – 2015), a board-certified in Internal Medicine (1964), completed subspecialty training in hematology and Oncology at John Hopkins University (1967). In 1967, he returned to his country as a faculty member at the Shiraz University of Medical Sciences. He was the founder of the Blood Transfusion Organization and bone marrow transplantation ward (1993) in Shiraz. He has published 56 articles and was a permanent member of the Academy of Medical Sciences since 2005.²⁶

In 1989, the first Hematology and Medical Oncology Ward in the southern part of Iran was opened in Namazi Hospital under the supervision of Dr. Haghshenas. The major activities were aimed at training hematology and medical oncology fellows admitted through entrance exam and interview, opening the first Bone Marrow Transplant Unit in the southern part of the country and second BMT center in Namazi Hospital. In order to enhance educational, research and treatment activities, Dr. Mani Ramzi pursued fellowship training program in oncology and stem cell transplantation in Switzerland and United States in 2000.

During 1993 – 2014, the number of patients receiving transplantation increased from 8 to 150 per year and the number of patients underwent transplantation reached 1030.

In 1961, the first radiotherapy ward as a subgroup of the radiology department was established in Namazi hospital²⁷ and medical oncology setting up the groundwork for cooperation was provided.

Educational curriculum in Hematology and Medical oncology in Iran Hematology and Medical Oncology was the first subspecialty approved by the Ministry of Health, Treatment and Medical Edu-



Figure 15. Dr. Eskandar Akhavan Zakeri, Faculty of Tehran University of Medical Sciences, Imam Khomeini Hospital Complex, one of the pioneers and first members of the Subspecialty Board of Hematology and Medical Oncology in Iran

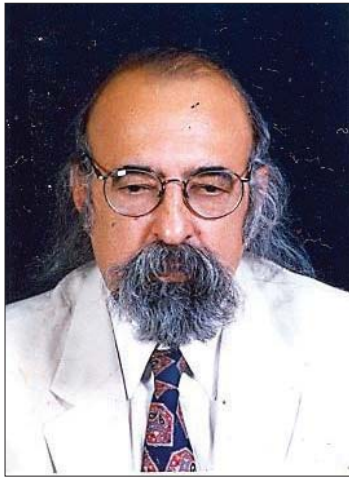


Figure 16. Dr. Jahangir Raafat, Medical Oncologist, faculty of Tehran University of Medical Sciences, Imam Khomeini Hospital Complex, Cancer Institute, one of the pioneers and first members of the Subspecialty Board of Hematology and Medical Oncology in Iran

cation in 1983 and board-certified internists were eligible to sit for a subspecialty exam in Hematology and Medical Oncology. The first members of the Subspecialty Board of Hematology and Medical Oncology in Iran include: Dr. Nasrollah Sayyar (Figure 14), Dr. Eskandar Akhavan Zackery (Figure 15), Dr. Davoud Monadzadeh, Dr. Ardeshir Ghavamzadeh (Figure 7) and Dr. Jahangir Raafat (Figure 16).

The new curriculum in Hematology and Medical Oncology in Iran created by ISMOH (Iranian Society of Medical Oncology and Hematology) in 2008. Some chapters in medical oncology part included cancer biology and genetics, cancer etiology, surgical and radiation oncology, chemotherapy, clinical research and bone marrow transplantation. Currently, subspecialty residents in Hematology and Medical Oncology are being trained at 6 universities in Iran (Tehran University of Medical Sciences, Tabriz University of Medical Sciences, Shahid Beheshti University of Medical Sciences, Shiraz University of Medical Sciences, Isfahan University of Medical Sciences and Mashhad University of Medical Sciences). Up to 2015, over 250 residents have been graduated from these universities. Hematologists and Medical Oncologists

are serving as academic members in all provinces and big cities in Iran.

Cancer Hospital in Iran

Improvement of health care system in Iran has led to pay more attention to non-infectious disorders such as different types of cancer. Therefore, the demand for specialized staff in the areas of cancer research, education and therapy has increased. To respond to these requirements, we can offer the construction of a cancer hospital at least in each provincial medical school.

Some parts of cancer hospital may include: Adult Hematology and Medical Oncology/ Pediatric Hematology and Oncology/ Hematopoietic Stem Cell Transplant/ Cancer Surgery/ Radiation Oncology/ Pathology and Molecular Diagnostic Testing/ Radiology/ Cancer Research Center/ Joint Clinics/ Centers for Cancer Control, Prevention and Screening/ Nuclear Medicine/ Palliative Care/ Psychology Oncology/ Social Worker.

These hospitals link together in networks to disseminate the latest information on cancer diagnosis, prevention and treatment, multicenter studies and knowledge improvement. The hospitals can follow the uniform guidelines. Cancer Institute of Tehran University of Medical Sciences is an example of the successful cancer hospital.

Briefly In 1960's, combination chemotherapy was developed for the treatment of acute leukemia, Hodgkin's lymphoma and invasive non-Hodgkin's lymphoma, facilitating the process of treatment in the patients with advanced malignancies. In 1970's, neo-adjuvant and adjuvant chemotherapies were used in the treatment of solid tumors and metastatic cancers.

Medical Oncology is a relatively new medical discipline in Iran, compared to developed countries. From 1987 to 2015, over 250 trainees graduated in the subspecialty of Hematology and Medical Oncology from 10 universities. They work in multidisciplinary teams (MDT) in all provincial capitals and other major cities in Iran. The ultimate goals of medical oncology in the future are early detection and prevention of cancer. On this basis, it appears that Cancer Hospital network and multidisciplinary teams can improve outcomes and survival in cancer patients as well as reducing health care costs in Iran.

Conflict of Interest: None

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