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History of Medicine in Iran

History of Multiple Sclerosis in Iran

Abdorreza Naser Moghadasi, MD[1*]

[1]Multiple Sclerosis Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Iran is a great country with a long history of civilization and medicine. Following the increase in the prevalence of multiple sclerosis (MS), Iranian scientists and physicians started considering this disease and its outcomes in Iran. The first MS paper published by Iranian scientists dates back to 1963, when a case of hereditary spastic ataxia mimicking MS was reported. With the cooperation of his colleagues, Prof. Jamshid Lotfi conducted the first MS-related paper. The Iranian MS Society was established in 1998 in Iran, and is currently a member of the MS International Federation (MSIF). Progressively, after the scientific development of Iranian universities and recognizing the importance of the disease, the first specialized MS ward was established in Sina hospital by Prof. Mohammad Ali Sahraian and was followed by the establishment of the first MS research center. MS Society is presently quite active and the Iranian MS congress is annually held in one of the Iranian universities to review the most recent achievements in the field of the disease. The present study aims to illustrate the history of the efforts made on the way, and attempts to introduce the people who took significant steps in this regard.

Keywords: History, Multiple Sclerosis, Iran

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Introduction

A Brief History of Medicine and Neurology in Iran

Iran, also known as Persia,[1] is one of the oldest civilizations in the world[2] with more than 7000 years of history. This civilization has been the origin of great progress in medicine throughout history. In this regard, a 4700-year-old human skull found in the Burnt City (Shahr-e-Sukhteh) is the evidence of the first skull surgery in Iran.[3] The skull which belonged to a 13-year-old girl suffering from hydrocephalus indicates that she had undergone cranial surgery to remove part of her skull bone, and it seems that the girl lived for at least about 6 months after the surgery. Also, the world's earliest artificial eyeball was found in this city.[4] The Iranian civilization is also famous for its brilliant medical history during the pre-Islamic period which is mentioned in Gathas of Zarathustra.[5] Actually, the earliest records of ancient Iranian medicine are seen in Zend Avesta and the Vendidad (the surviving texts of Avesta) which differentiate three kinds of healing: healing by knife (surgery), healing using the herbs, and healing by uttering the divine words.[6] Although many schools, universities, and libraries were destroyed following the Arab invasion of Iran, the major growth and flourishing in medical science in Iran occurred in the post-Islamic era, following the emergence of scientists and physicians like Avicenna and Mohammad Zakaria Razi. The Iranian-Islamic traditional medicine based on books like Canon of Medicine and The Virtuous Life (*al-Hawi*) is still dynamic and active in Iran.[7]

Neurology was developed in Iran during the Islamic era when Iranian physicians made incredible progress in fields of headache and convulsion.[8,9] Perhaps it can be said that Avicenna was the most prominent Iranian physician who could significantly change our understanding of neurological diseases. He devoted the third part of his book to neurological diseases. In the first section, he discusses the anatomy of the nervous system and signs and symptoms in the field of neurology. In the second section, concerning headache, he categorizes 27 types of headaches and explains how to manage and control them.[8] For the first time, he described some diseases including meningitis.[10] He was even the originator of new methods in neurosurgery.[11] He described diseases like hydrocephalus more precisely and differentiated it from intracerebral hemorrhage.[12]

The modern medicine was chiefly formed after the establishment of *DĀR AL-FONŪN* by Amir Kabir, followed by the foundation of the first modern hospital of Iran called "State Hospital (*Marizkhaneh-ye-Dowlati*)" (today's Sina Hospital) (Figure 1).[13]

Modern neurology in Iran owes its foundation and establishment to the restless efforts done by many physicians well-trained in the West such as professors Barimani (Figure 2), Lotfi, Pakdaman (Figure 3), and so on. Professor Jalal Barimani, known as the father of modern neurology in Iran, published the first Iranian neurology papers in international journals and was the main representative of Iranian neurologists in international meetings and congresses.[14,15] He was born in 1308 in Sari. In 1339, he obtained a specialized degree in psychology

*Corresponding Author: Abdorreza Naser Moghadasi, MD; Sina MS Research Center, Sina Hospital, Tehran University of Medical Sciences, Hasan Abad Sq., Tehran, Iran. Tel: +98-21-66348571; Fax: +98-21-66348570; Email: abdorrezamoghadasi@gmail.com

Figure 1. The State Hospital (Today's Sina Hospital).

Figure 2. Prof. Jalal Barimani.

Figure 3. Prof. Hossein Pakdaman.

and neuroscience from Paris University. He is also the founder of the Neurology Research Center at Tehran University of Medical Sciences.

He wrote more than 200 papers in French, English, and Persian on neurology, clinical neurophysiology, and literature. In addition, "History of Iran-France Medical Relations" (compiled in French and Persian) and "In the Sky of Literary" (compiled in Persian) are among his published works.

He retired in 1987 as the head of the Department of Neurology at Tehran University of Medical Sciences. He became a full-professor in 1970, and after providing sincere services to the Iranian medical society for many years, he passed away in early March 2012.[16]

Neurology is now a well-recognized branch of medicine in Iran, and about 1000 neurologists are practicing throughout the country.

Epidemiology of MS in Iran

Multiple sclerosis (MS) is a chronic disease causing several neurologic symptoms following the involvement of myelin. In Iran, the first epidemiological study was conducted by Prof. Etemadifar in Isfahan in 2006. The prevalence of MS in Isfahan was reported to be 35.5 per 100 000 persons, with a female to male ratio of 3.9%.[17] According to the research carried out in 1975[18] and 1980,[19] Iran was previously a region with low incidence of MS; however, recent research has revealed that it has recently become a region with a high prevalence of MS.[20]

In a study published in 2014, the prevalence rate of the disease in Tehran was 101.39: 100 000 persons.[21]

Briefly, this change is mainly the result of factors such as lifestyle changes, urbanization, industrialization, and modernization. Other reasons include the lack of vitamin D intake, economic growth and changes in living standards, smoking, air pollution, and occupational and non-occupational contacts with chemicals[22].

The average age of patients was reported to be 27.24 years[20] which was also confirmed in other studies. With respect to the high prevalence of MS and its increasing growth, paying due attention to the disease and the patients' needs has become a significant objective of the medical society in Iran, and numerous attempts are being made correspondingly. Despite the national efforts made in this regard, there are still some problems. It seems that sympathy and patience would be the key to overcoming the challenges. The present study aims to illustrate the history of the efforts made on the way, and attempts to introduce the people who took significant steps in this regard.

History of MS in Iran

MS Cases in Old Persian Medicine

New studies show that, Ali ibn al-'Abbas al-Majusi, author of *al-Maliki* (Complete Book of the Medical Art) and Ibn Rushd could explain optic neuritis and paresthesia as well as their relationship in their works.[23] Explanation of the relationship can be considered as the first description of MS-related symptoms in the world's medical history. Interestingly, they had correctly diagnosed that the blurredness (presently called optic neuritis) is caused by inflammation and obstruction of the optic nerve.[23] Al-Majusi took further steps and stated that any inflammation or obstruction causing optic neuritis can be the possible cause of paresthesia.[23]

The First Iranian Publication on Multiple Sclerosis

The first published Iranian work in relation to MS dates back to 1963.

In 1963, MS, then referred to as "disseminated sclerosis", was first mentioned in a paper written by Dr. Mohsen Mahloudji (Figure 4) which was published in the *Psychiatry Neurology Neurosurgery Journal*.[24] In the paper, three members of a family with hereditary spastic ataxia were described whose symptoms could be mistaken as disseminated sclerosis; but due to the positive family history, the proper diagnosis would be hereditary spastic ataxia. The study was conducted in Namazi Hospital, Shiraz, Iran.

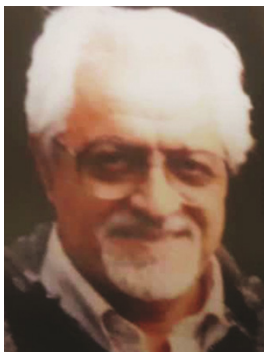

Figure 4. Dr. Mohsen Mahloudji (special thanks to Dr. Abbas Nemati).

Figure 5. Prof. Jamshid Lotfi.

The First Citation Regarding Iranian MS Patients

The first reference made to Iranian MS patients was in a paper entitled, "Multiple Sclerosis among Immigrants in Greater London" which was published in the *British Medical Journal* in 1976. In the paper, the prevalence rate of MS was discussed among immigrants in London, and the percentage of patients hospitalized with MS was mentioned to be high or average high among Iranian immigrants (similar to Turkish, Egyptian, Australian, and South American immigrants).[25]

Subsequent reports also mentioned the MS prevalence among Iranians residing in India who immigrated 1000 years ago and were known as Parsis.[26] In a report published on Bombay Parsis, the prevalence rate of MS was reported to be 21:100 000.[26] In another study carried out on the Persians inhabiting in Bombay and Pune, MS prevalence rate among Persians was reported to be much higher than the rate among Indians (26:100 000 in Bombay & 58:100 000 in Pune).[27]

The First MS-Related Article Published by an Iranian Scientist

The first MS paper entitled, "Histocompatibility Antigens (HLA) in Multiple Sclerosis in Iran" which was written by Prof. Jamshid Lotfi et al was published in the *Journal of Neurology, Neurosurgery and Psychiatry*.[28] In this paper, the prevalence rate of Locus A and B in HLA system of MS patients was compared with a control group. The results of this study showed that the prevalence of HLA A3, HLA A11, and HLA B7 was significantly higher in MS patients than the control group (Figure 5).[28]

Establishment of Iran's Multiple Sclerosis Society (IMSS) in 2001

Considering the increasing growth of MS in the Iranian society, establishing an association for outsourcing the affairs of MS patients seemed quite necessary. This was also followed by some whose family members or friends were MS patients. Finally, a room was allocated to the association in the Charity Foundation for Special Diseases of Iran which was supported by Mrs. Fateme Hashemi. The MS Society owes its birth to the attempts of Mrs. Nia (Soltani), Mrs. Kharazi (Asgari) and Mrs. Mohseninia (Davoudi). Following a few meetings, the members of the establishing board including Prof. Jamshid Lotfi, Prof. Hajir Sigaroodi, Mr. Mohsen Asayesh, and Mr. Majid Ghomi were nominated, and then different committees were formed. Scientific, executive, and financial committees of the society had a meeting with MSIF delegates, Paul Williams and Michael Dynin, and it officially joined the federation in 2001. The scientific committee of the Iranian MS society was established by Prof. Masoud Nabavi, and then managed by Prof. Maryam Noroozian (2000-2002), Prof. Mohammad Ali Sahraian (2002–2011), and Prof. Mohammad Reza Motamed (since 2011). During the recent years, the society has undergone many changes. IMSS has held 16 international MS congresses (annual seminars for MS Day on the last Wednesday of May), assisted patients with their medication costs considering the restricted budget of the society, established active relationships with relevant organizations to further contribute to the patients, and conducted research projects leading to improvements in the patients' life quality. Also, the society has a monthly publication called "MS Message" since 2003. Currently, the society has nearly 75 000 members.[29]

The first Iranian patient officially registered by the IMSS was a 70-year-old man whose disease was developed in 1969 when he was 25 years old. He presented with left limb paresthesia. His cerebrospinal fluid was studied due to the absence of appropriate imaging methods at that time. The first magnetic resonance imaging was performed on him in 1995, and the patient turned into the secondary progressive form in 2001. The patient is currently being treated and is regularly in touch with the IMSS (The patient information was obtained from the MS Society of Iran and through an interview with the patient. The patient's consent was gained for publishing the information).

The First MS Congress in Iran Was Held in 2004

In Iran, the first MS congress was held in the Imam Hall of

Imam Khomeini University Hospital, Tehran University of Medical Sciences on November 29, 2004. Prof. Sahraian was the director of the first MS congress.

The congress was held with the contribution of the IMSS and Tehran University of Medical Sciences. Since then, the congress has been held annually, and there have already been 16 congresses following the kind cooperation of national universities, MS research center, and different MS societies (Information on the first MS Congress in Iran was obtained through archives of MS Society of Iran).

The First Iranian MS Biosimilar Drug Was Produced in 2006

Cinnovex is the first Iranian MS biosimilar drug produced in CinnaGen Company (founded in 1994) in cooperation with the Fraunhofer Institute, Germany. The production of the first recombinant product initiated in 2003 which entered the market in 2006. Cinnovex is Interferon beta-1α similar to Avonex, and has been used by approximately 11 000 patients.[30]

The First MS Fellowship in Iran Graduated from the University Hospital of Basel in 2006 and Returned to Iran

In Iran, the first formal MS fellowship was completed by Prof. Mohammad Ali Sahraian (Figure 6) who performed his neurology residency at Sina Hospital, Tehran University of Medical Sciences. He passed his training courses on MS in the University Hospital of Basel, Switzerland. Co-authorship in Atlas of MS lesions with Prof. E. W. Radue was one of the significant activities of Prof. Sahraian during his fellowship period.[31] After returning to Iran, Prof. Sahraian made great contributions to the field of MS in Iran. Now, he is the vice president of the IMSS and the head of MS Research Center in Sina hospital.

The First Specialized MS Ward in Iran Was Established in 2007

The first specialized MS ward of Iran was established in Sina Hospital in 2007 with five inpatient care beds and five beds for outpatient services. This ward was developed after moving to the new building of Sina Hospital, and now has nine and six beds for women and men, respectively (Information on the first MS ward and Research center in Iran was obtained through interviews with authorities of Sina Hospital).

Figure 6. Prof. Mohammad Ali Sahraian.

The First MS Research Center in Iran Was Established in 2009

Along with the establishment of the first specialized MS ward in Iran, the first MS Research Center was founded by Prof. Sahraian in September 2009. The center gradually developed its activities and now has different research groups working on several MS-related fields, the most important of which include cognitive, imaging, and epidemiology groups. The MS research center is now affiliated to the Neuroscience Institute, Tehran University of Medical Sciences. The center has participated in many national trials and has been one of the leaders regarding MS education in the country. An outpatient department also exists which provides clinical services to MS patients. The MS Research Center ranked first in Razi research festival in 2018.

Current Status of MS in Iranian Universities and Medical Centers

MS is presently considered a great concern in the universities and research centers of Iran. With respect to the growing prevalence of MS in Iran and the involvement of young generation, special attention should be paid to this issue. Many skillful physicians, especially at universities of medical sciences have devoted their lives to improving the conditions of the patients, and have conducted numerous research projects in this regard. Furthermore, following the production of biosimilar Cinnovex, other pharmaceutical companies have directed their activities toward manufacturing other related drugs such as ReciGen, Ziferon, Copamer, and Osvimer.

The MS-Related Papers Published until March 2019

Iranian scientists have published several papers on various aspects of MS. By April 2019, more than 1450 papers were found on different aspects of the disease including epidemiology, genetics, risk factors, imaging, medication side effects, and symptomatic treatments. The information was obtained through searching the PubMed database.

MS Fellowship in Iran

Based on an agreement with the Ministry of Health, Treatment, and Medical Education, the first MS fellowship program was launched in Sina hospital with the cooperation of Imam Khomeini Hospital which is affiliated to Tehran University of Medical Sciences. The fellowship was run by a team headed by Prof. Sahraian. Dr. Seyed Mohammad Baghbanian and Dr. Hamidreza Ghalyanchi were the first accepted fellows. Applicants

are admitted following oral and written examinations. The program takes 12 months during which the fellows will become familiar with different aspects of the disease including treatment, imaging features, and diagnostic tests.[32]

Future Prospects

In spite of all the above-mentioned efforts, it seems that the steps taken so far are primary and more should be done to improve MS patients' quality of life. Since MS is a complicated disease involving different biological, psychological, and social aspects of one's life, one of the major concerns is the need for maintaining close cooperation among different clinical groups including neurologists, psychiatrists, psychologists, nutritionists, physiotherapists, and social workers to further provide quality services to these patients. However, there is no center in Iran covering all these needs. In fact, considering the increasing prevalence of the disease in Iran and the growing number of patients, founding such a clinic would only be possible in the form of a national project.

Conflict of Interest Disclosures

None to be declared.

Ethical Statement

This study is based on Committee on Publication Ethics' rules.

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