

# Status of clinical toxicology education and ethics in medical care of poisoned patients in the Islamic Republic of Iran and a comparison with other countries

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## Abstract

Clinical toxicology is not recognized as a clinical speciality in Iran. After the chemical war gas attack by the Iraqi army against the Iranian troops in the 1980s, health professionals and Iranian authorities noticed the importance of this field in clinical medicine. Collaboration between the clinical toxicologists and toxicologists of pharmacy schools resulted in the establishment of the Iranian Society of Toxicology and Poisonings in 1991 and the National Board of Toxicology in 1993. Clinical toxicology fellowship was also formed as a joint collaboration between the toxicology and internal medicine boards in 2010. Medical doctors who specialized in clinical medicine are eligible to take the entrance examination of the fellowship. In spite of the advancement of clinical toxicology and increased number of acute poisonings and drug abuse, undergraduate teaching in this field is still lacking and being taught as part of the forensic medicine curriculum since 1952. There is a lack of an efficient national poison information and control centre (s) in Iran, and no action plan and practical efforts have been done for poisoning prevention. Therefore, the number of drug abuse and acute poisonings has increased over the past four decades and induced cultural, social and health problems. According to Iranian legal medicine organization reports, poisoning is the second-most occurring cause of unnatural death. The suicidal attempt is the most common method of acute poisoning in adults. Suicidal attempt including self-poisoning is not accepted in the Islamic point of view, and thus self-poisoning is mostly neglected and may not be treated appropriately in time in some regions of Iran. Accidental poisoning in children is also common in Iran and estimated to be between 20 000 and 25 000 cases annually over the recent years. In addition, social, cultural and economic problems have induced more health problems such as drug abuse and addiction even in children. Adulterated opium to lead for economic gaining has produced thousands of cases of lead poisoning over the past few years in nearly all opium addicts, which is still a major health problem in Iran. Ban on alcoholic beverages leads some people to make their own home-made spirits, which is unfortunately contaminated with methanol. Thousands of cases of methanol poisoning and even some epidemics have occurred over the past four decades in some parts of the country. Lack of availability of essential antidotes such

as succimer and fomepizole has been a major problem for the effective treatment of poisoned patients. Despite the well-known fact that cases of poisoning and drug overdose constitute a significant proportion of hospital admissions in some developing countries, clinical toxicology education and medical care of the poisoned patients are lacking. Therefore, policymakers and health authorities should realize the importance of toxicology in clinical medicine. The Iranian Ministry of Health, medical care and Medical Education should implement clinical toxicology courses for medical students; establish effective national poisons information and control centres and advance clinical toxicology services for appropriate management of poisoned patients to improve public health and the overall health policy goals.

#### KEYWORDS

clinical toxicology, Iran, medical care, medical education, poisoning

## 1 | INTRODUCTION

Clinical toxicology is not recognized as a clinical speciality in Iran. After the chemical war gas attack by the Iraqi army against the Iranian troops in the 1980s, health professionals and Iranian authorities noticed the importance of this field in clinical medicine. At the time, there were only very few clinical toxicologists in Iran. Basic and pharmaceutical toxicology has long been established in the pharmacy schools, but not in medicine.

## 2 | ESTABLISHMENT OF SOCIETY OF TOXICOLOGY, NATIONAL BOARD AND FELLOWSHIP

The collaboration between the clinical toxicologists and toxicologists of pharmacy schools resulted in the establishment of Iranian Society of Toxicology and Poisonings in 1991 and National Board of Toxicology in 1993.

Clinical toxicology fellowship was also formed as a joint collaboration between the toxicology and internal medicine boards in 2010. Medical doctors specialized in clinical medicine are eligible to take the entrance examination of the fellowship. The qualified clinical toxicology centres in Mashhad, Tehran and Isfahan trained fellows over the years that are now academic members of universities of medical sciences in Iran.

## 3 | PROBLEMS OF EDUCATION AND POISONS CONTROL

In spite of the advancement of clinical toxicology and increased number of acute poisonings and drug abuse,

undergraduate teaching in this field is still lacking and being taught as part of the forensic medicine curriculum since 1952.

Lack of efficient national poison information and control centre(s) in Iran and no action plan and practical efforts have been done for poisoning prevention. Therefore, the number of drug abuse and acute poisonings has increased over the past four decades and induced cultural, social and health problems.<sup>1-4</sup>

According to Iranian legal medicine organization reports, poisoning is the second cause of unnatural death.<sup>5-8</sup> Suicidal attempt is the most common method of acute poisoning in adults.<sup>1-4</sup>

## 4 | LACK OF MEDICAL ETHICS

Suicidal attempt including self-poisoning is prohibited in Islamic point of view and thus self-poisoning is mostly neglected and may not be treated appropriately in time in some regions of Iran.<sup>8,9</sup> However, the medical and nursing staff based on humanitarian, ethical and legal duty try to treat the patients, despite the lack of facilities.

It will be difficult to overcome a cultural intolerance of suicide, but perhaps philosophical arguments explaining the nature of mental illness could help with mitigation.

## 5 | POISONING IN CHILDREN

Accidental poisoning in children is also common in Iran and estimated between 20 000 and 25 000 cases annually over the recent years.<sup>10</sup> The complexity and increasing production of various chemicals and medicines, unsafe packaging, lack of general information, random errors in prescription, environmental pollution, social and economic crises, inadequate child care, availability of natural toxins (toxic plants and venomous

**TABLE 1** Comparison of the status of clinical toxicology between Iran and some African countries<sup>22,24-29</sup>

Country	Undergraduate teaching	Poisoning treatment centre	National poison information/control centre/service	Medical toxicology (MSc, PhD)	Clinical toxicology (speciality/fellowship)	National board of toxicology	Society/Academy of toxicology
1 I.R.Iran	Yes, but not enough	Yes	Yes But not efficient	Yes	Yes, Fellowship since 2010	Yes, since 1993	Yes, Iranian Society of Toxicology since 1990
2 Algeria	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
3 Angola	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
4 Cameroon	U/ND	U/ND	U/ND	U/ND	U/ND	U/ND	Yes
5 Egypt	Yes	U/ND	Yes	U/ND	Yes	U/ND	Yes, Egyptian Society of Toxicology
6 Ghana	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
7 Kenya	Yes	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
8 Morocco	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
9 Nigeria	Yes	U/ND	U/ND	U/ND	U/ND	U/ND	Yes
10 Senegal	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
11 South Africa	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes
12 Tanzania	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
13 Tunisia	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
14 Zimbabwe	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND

Abbreviation: U/ND: Unavailable/no data.

animals), false traditions and superstitions have caused child poisonings in Iran over the past four decades. In addition, social, cultural and economic problems have induced more health problems such as drug abuse and addiction even in children.<sup>10</sup> Also in recent years, some reports indicated unwanted poisoning or even death of children by medications used for addiction therapy (eg methadone or buprenorphine).

## 6 | EPIDEMIC OF LEAD AND METHANOL POISONINGS

Adulterated of opium to lead for economic gaining have produced thousands of cases of lead poisoning over the past few years in nearly all opium addicts, which is still a major health problem in Iran. Ban on alcoholic beverages led some people to make their own home-made spirits, which is unfortunately contaminated with methanol. Thousands of cases of methanol poisoning and even some epidemics have occurred over the past four decades in some parts of the country. The economic crisis in recent months—particularly on foreign currency—has urged alcohol users to get the home-made spirits. Producers of the home-made spirits do not remove the cellulosic parts of raw materials (grape seeds, date seeds, etc) and thus methanol

is produced in a large amount after distillation. The biggest epidemic has recently occurred in various cities with several hundreds of methanol-intoxicated patients and nearly a 10% mortality.<sup>11,12</sup> No official statistic has yet been reported as it is still going on. Lack of availability of essential antidotes such as succimer and fomepizole has been a major problem for the effective treatment of the poisoned patients.

## 7 | COMPARISON OF CLINICAL TOXICOLOGY STATUS OF IRAN WITH OTHER COUNTRIES

Currently, poisoning is a significant global public health problem.<sup>13</sup> Human poisoning has, however, been a problem since ancient times, but until after World War II, it was unusual.<sup>14</sup> In the United States, medical and clinical toxicology is a field of medicine and medical toxicologists are medical doctors who specialize in the prevention, education and management of injury and illness from xenobiotics or exposure to biological and radiological agents.<sup>15-18</sup> Clinical toxicology is a rapidly evolving field with new information emerging daily, and in some countries such as the UK and United States, poisoning ranks among the top 10 reasons for hospital admission.<sup>13,17,18</sup>

**TABLE 2** Comparison of the status of clinical toxicology between Iran and some countries of the Americas<sup>22,25-34</sup>

Country	Undergraduate teaching	Poisoning treatment centre	National poison information/control centre/service	Medical toxicology (MSc, PhD)	Clinical toxicology (speciality/fellowship)	National board of toxicology	Society/Academy of toxicology
1 I.R. Iran	Yes, but not enough	Yes	Yes But not efficient	Yes	Yes, Fellowship since 2010	Yes, since 1993	Yes, Iranian Society of Toxicology since 1990
2 USA	Yes	Yes	Yes, since 1954	Yes	Yes, since 1993	Yes, since 1974	Yes, American Academy of Clinical Toxicology and many societies
3 Argentina	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes, Argentine Toxicology Association
4 Brazil	U/ND	Yes	Yes	U/ND	U/ND	U/ND	Yes, Brazilian Society of Toxicology
5 Cambodia	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
6 Canada	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes (STC)
7 Chile	Yes	U/ND	Yes	U/ND	U/ND	U/ND	Yes (STC) (ALATOX)
8 Colombia	U/ND	U/ND	U/ND	U/ND	U/ND	U/ND	Yes (CST)
9 Costa Rica	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
10 Cuba	U/ND	U/ND	Yes	U/ND	Yes	U/ND	Yes (TCS)
11 Ecuador	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
12 Guatemala	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
13 Jamaica	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
14 Mexico	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes (SMT)
15 Nicaragua	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
16 Paraguay	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
17 Peru	Yes	U/ND	U/ND	U/ND	U/ND	U/ND	Yes
18 Puerto Rico	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
19 Trinidad and Tobago	U/ND	Yes	Yes	U/ND	U/ND	U/ND	U/ND
20 Uruguay	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	Yes
21 Venezuela	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND

Abbreviation: U/ND: Unavailable/no data.

## 8 | STATUS OF CLINICAL TOXICOLOGY IN THE UK

Many years ago, the emergence of clinical toxicology in Edinburgh resulted primarily from government concerns over the increasing numbers of individuals throughout Britain poisoning themselves. As a consequence, in 1962, they issued the Atkins Report which recommended the establishment of poisoning treatment centres and poisons information services.

Therefore, a Regional Poisoning Treatment Centre and Scottish Poisons Information Service were established in the Royal Infirmary of Edinburgh.<sup>14</sup>

Some years later, London and Birmingham also considered clinical toxicology as an important issue. A Poisons Information Centre opened in London as well as a clinical ward for poisoned patients in Birmingham. Coordination of the British clinical toxicologist via the National Health Service resulted in the establishment of the National Poisons

**TABLE 3** Comparison the status of toxicology between Iran and the Asian continent<sup>22,25-29,35-42</sup>

Country	Undergraduate teaching	Poisoning treatment centre	National poison information/control centre/service	Medical toxicology (MSc, PhD)	Clinical toxicology (speciality/fellowship)	National board of toxicology	Society/Academy of toxicology
1 I.R. Iran	Yes, but not enough	Yes	Yes But not efficient	Yes	Yes, Fellowship since 2010	Yes, since 1993	Yes, Iranian Society of Toxicology since 1990
2 Bangladesh	U/ND	U/ND	U/ND	U/ND	U/ND	U/ND	Yes
3 China	Yes	Yes	Yes	U/ND	Yes	U/ND	Yes
4 India	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes
5 Indonesia	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
6 Iraq	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
7 Israel	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	Yes
8 Japan	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9 Jordan	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
10 Kazakhstan	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
11 Korea	Yes	Yes	Yes	U/ND	Yes	Yes	Yes
12 Lebanon	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
13 Malaysia	Yes	Yes	Yes	U/ND	Fellowship	Yes	Yes
14 Mongolia	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
15 Myanmar	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
16 Nepal	Yes	U/ND	Yes	U/ND	U/ND	U/ND	Yes
17 Oman	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
18 Pakistan	Yes	Yes	Yes	U/ND	Yes	U/ND	U/ND
19 Palestinian Territories	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
20 Philippines	U/ND	Yes	Yes	U/ND	U/ND	U/ND	U/ND
21 Saudi Arabia	U/ND	Yes	Yes	U/ND	U/ND	U/ND	U/ND
22 Sri Lanka	U/ND	Yes	Yes	MSc Fellowship	U/ND	U/ND	U/ND
23 Singapore	Yes	U/ND	U/ND	U/ND	U/ND	U/ND	Yes
24 Syria	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
25 Taiwan	Yes	U/ND	Yes	U/ND	Yes	Yes	Yes
26 Thailand	Yes	Yes	Yes	U/ND	Fellowship	U/ND	Yes
27 United Arab Emirates	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
28 Viet Nam	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND

Abbreviation: U/ND: Unavailable/no data.

Information Service (NPIS) that are predominately based in the poisons centres of London, Birmingham, Newcastle, Cardiff and Edinburgh. In the UK, clinical toxicologists are often invited by the government bodies and organizations to advise on the wider impact of poisonings, including public health policies. Moreover, clinical toxicologists contribute to all of NPIS roles, and also act as medicolegal expert witnesses in legal cases.<sup>17</sup>

## 9 | STATUS OF CLINICAL TOXICOLOGY IN THE UNITED STATES

In 1968, The American Academy of Clinical Toxicology (AACT) was founded for advancing the diagnosis and safe treatment of human and animal poisoning in the United States. In 1974, AACT established the American Board of Medical

**TABLE 4** Comparison of the status of clinical toxicology between Iran and some European countries<sup>22,25-29,43-53</sup>

Country	Undergraduate teaching	Poisoning treatment centre	National poison information/control centre/service	Medical toxicology (MSc, PhD)	Clinical toxicology (speciality/fellowship)	National board of toxicology	Society/Academy of toxicology
1 I.R. Iran	Yes, but not enough	Yes	Yes But not efficient	Yes	Yes, Fellowship since 2010	Yes, since 1993	Yes, Iranian Society of Toxicology since 1990
2 Albania	U/ND	U/ND	U/ND	U/ND	U/ND	U/ND	Yes
3 Austria	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes
4 Azerbaijan	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
5 Belarus	U/ND	Yes	Yes	U/ND	U/ND	U/ND	U/ND
6 Belgium	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes
7 Britain (UK)	Yes	Yes	Yes	Yes	Yes Speciality— PhD	U/ND	Yes
8 Bulgaria	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	Yes
19 Croatia	U/ND	Yes	Yes	U/ND	U/ND	U/ND	Yes
10 Czech Republic	U/ND	Yes	Yes	U/ND	U/ND	U/ND	YES
11 Denmark	U/ND	Yes	Yes	U/ND	U/ND	U/ND	Yes
12 Estonia	Yes	Yes	Yes	U/ND	MSc	U/ND	Yes
14 Finland	Yes	Yes	Yes	U/ND	Yes	Yes	Yes
15 France	Yes	Yes	Yes	U/ND	Yes	Yes	Yes
16 Georgia	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
17 Germany	Yes	Yes	Yes	U/ND	Yes		Yes
18 Greece	Yes	Yes	Yes	U/ND	Yes	Yes	Yes
19 Hungary	U/ND	Yes	Yes	U/ND	U/ND	U/ND	Yes
20 Iceland	U/ND	Yes	Yes	U/ND	U/ND	U/ND	U/ND
21 Ireland	U/ND	Yes	Yes	U/ND	U/ND	U/ND	Yes
22 Italy	U/ND	Yes	Yes	U/ND	U/ND	YES	Yes
23 Latvia	Yes	U/ND	U/ND	U/ND	MSc	U/ND	Yes
24 Lithuania	Yes	Yes	Yes	U/ND	MSc	U/ND	
25 Macedonia	U/ND	Yes	Yes	U/ND	U/ND	U/ND	Yes
26 Malta	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	U/ND
27 Netherlands	Yes	Yes	Yes 1949	U/ND	Fellowship -PET (Postgraduate Education in Toxicology) PhD	U/ND	Yes
28 Norway	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes
29 Poland	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes
30 Portugal	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes (SPF)
31 Romania	U/ND	U/ND	Yes	U/ND	U/ND	U/ND	Yes
32 Russia	U/ND	Yes	Yes	U/ND	U/ND	U/ND	Yes
33 Serbia	Yes	U/ND	Yes	U/ND	U/ND	U/ND	Yes

(Continues)

**TABLE 4** (Continued)

Country	Undergraduate teaching	Poisoning treatment centre	National poison information/control centre/service	Medical toxicology (MSc, PhD)	Clinical toxicology (speciality/fellowship)	National board of toxicology	Society/Academy of toxicology
34 Slovakia	Yes	Yes	Yes	U/ND	Yes	U/ND	Yes
35 Slovenia	Yes	Yes	Yes	U/ND	U/ND	U/ND	Yes
36 Spain	Yes	Yes	Yes	U/ND	Yes	U/ND	Yes
37 Sweden	Yes	Yes	Yes	U/ND	Postgraduate courses	U/ND	Yes
38 Switzerland	Yes	Yes	Yes	U/ND	M.Sc. course	U/ND	Yes
39 Turkey	Yes	Yes	Yes	U/ND	Yes Speciality	Yes	Yes
40 Ukraine	U/ND	U/ND	U/ND	U/ND	U/ND	U/ND	Yes

Abbreviation: U/ND: Unavailable/no data.

Toxicology (ABMT) to certify physicians in the speciality of clinical toxicology.<sup>15</sup> During the late 1970s and 1980s, fellowships in Medical Toxicology were organized all over the United States. During 1975-2000, the fellowships were not yet approved by the Accreditation Council for Graduate Medical Education (ACGME).<sup>15</sup> The American College of Medical Toxicology (ACMT) was the primary organization to serve physicians who are Medical Toxicologists, and in 2000, ACGME began to credential fellowship training in Medical Toxicology.<sup>16</sup>

## 10 | COMPARISON OF THE STATUS OF CLINICAL TOXICOLOGY IN IRAN WITH OTHER COUNTRIES

Although clinical toxicology is an essential part of medical care and education in developed countries,<sup>14-20</sup> it has not been applied in Iran<sup>21</sup> and some other developing countries.

Unfortunately, the field of poisonings has always been neglected. Even in referral hospitals for poisoned patients in most provinces, appropriate toxicological laboratory equipment and proper antidotes do not exist.<sup>12,21</sup> Over the past decades, there has been limited progress in establishing poisons centres, and as of February 2019, only 47% of member states had a poisons centre, with the most notable gaps being in the African, Eastern Mediterranean and Western Pacific regions.<sup>22</sup> Allocation of resources in the field of medical toxicology can significantly improve medical care and treatment of patients. In the developing countries, for example Iran, political policy on the healthcare priorities directed resources towards some medical fields which do not necessarily improve the general health care and patients' survival. Many poisoned patients are among the most deprived and vulnerable groups of the community who are usually neglected.<sup>21,23</sup>

Comparisons of the clinical toxicology status between Iran and some other countries of the five continents are summarized in Tables 1-5. As can be seen in the tables, in spite

**TABLE 5** Comparison of the status of clinical toxicology between Iran and Pacific countries<sup>22,25-29</sup>

Country	Undergraduate teaching	Poisoning treatment centre	National poison information/control centre/service	Medical toxicology (MSc, PhD)	Clinical toxicology (speciality/fellowship)	National board of toxicology	Society/Academy of toxicology
1 I.R. Iran	Yes, but not enough	Yes	Yes But not efficient	Yes	Yes, Fellowship since 2010	Yes, since 1993	Yes, Iranian Society of Toxicology since 1990
2 Australia	Yes	Yes	Yes	U/ND	Yes	U/ND	Yes
3 New Zealand	U/ND	Yes	Yes	U/ND	U/ND	U/ND	U/ND

Abbreviation: U/ND, Unavailable/no data.

of the WHO advice, help and recommendation and also individual efforts of clinical toxicologists, medical education and clinical care of poisoned patients in most developing countries are very poor.

## 11 | CONCLUSION AND RECOMMENDATION

Attention to the International human rights, medical ethics and patient rights may improve clinical management of poisoned patients in developing countries such as Iran. It is essential that scholars of social media and health authorities pay more attention to the field of poisoned patient ethics, to change the attitudes of people and officials towards appropriate management of these patients.

Despite the well-known fact that cases of poisoning and drug overdose constitute a significant proportion of hospital admissions,<sup>21,23</sup> in some developing countries, clinical toxicology education and medical care of the poisoned patients are lacking. Therefore, the policymakers and the health authorities should realize the importance of toxicology in clinical medicine. The Iranian Ministry of Health and Medical Education should implement clinical toxicology courses for medical students; establish effective national poisons information and control centres and advance clinical toxicology services for appropriate management of poisoned patients to improve public health and the overall health policy goals.<sup>12,21,23-25</sup> This can also be applicable in other developing countries.

### CONFLICT OF INTEREST

None.

### AUTHORS' CONTRIBUTION

The first author (Ali Banagozar-Mohammadi) had the idea and prepared a first draft of the manuscript and further revision. The corresponding author (Mahdi Balali-Mood) expanded the idea, reviewed and revised the manuscript several times. The other three authors (Anahita Alizadeh, Mohammad Delirrad and Mohammad Majidi) prepared parts of revision and reviewed the manuscript.

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